THE PRACTITIONER

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THE MONTH

THE changing picture of industrial medicine is well brought out this month by the symposium on "Occupational Diseases". A generation ago beryllium was a scientific curiosity; to-day it constitutes an important industrial hazard. "Occupational jaundice and anæmia", on the other hand, represents a problem first brought to the fore during the 1914-18 war, which still requires careful watching to keep it under control. The problem of "occupational carcinogenesis" is important, not only from the point of view of industry, but also from the larger angle of the underlying cause of malignant disease. "Occupational dermatoses" is a summary of a problem which continually crops up in the day-to-day work of the practitioner in industrial districts, and he will also learn much of practical value from the article on "industrial law for the general practitioner". Finally, but by no means least in importance there is "vocational psychology", a branch of industrial medicine which has received an important fillip from the work on vocational selection carried out during the 1939-45 war.

The Symposium

IN the days when medicine was an art, and not a science, and when patients were individuals, and not cases, physicians preferred to couch their advice and instructions in homely terms which could be understood by their patients. Hence the prescribing of medicines in terms of spoonsful rather than more precise terms. The lack of any standard for the capacity of spoons was known, but the variations were of little practical import when the bulk of medicine consisted of galenicals made up in mixtures of such a strength that the therapeutic dose was well below the toxic dose. The advent of the potent synthetic drugs has diminished this margin to such an extent that, if spoons are to continue as the standard method of administering medicines, some standardization is called for. The problem has been brought to a head recently by the action of the British Standards Institution in issuing specifications for the capacity of domestic teaspoons and tablespoons which conform with American specifications. As the American fluid ounce is larger than the Imperial fluid ounce, this has meant an increase in the capacity of spoons which might lead to serious consequences in their use for taking medicines.

Medicinal Spoons

In response to representations by the Pharmaceutical Society and the Ministry of Health, the British Standards Institution has now issued specifications (B.S. 1348:1949) for spoons used in measuring medicine.

They are to be elliptical in shape, coloured red, and made of glass, china, chromium-plated metal, or certain prescribed plastic materials. The handles must be strong enough to permit the scooping of viscous substances without bending, and each spoon must bear indelibly the word "medicine". The levelled capacity of medicine tablespoons is to be 1/40 of an Imperial pint, or 240 minims (the capacity of the new cookery tablespoon is to be 1/32 of an Imperial pint). The levelled capacity of the medicine teaspoon is to be 1/160 of an Imperial pint, or 60 minims (the capacity of the new cookery teaspoon is to be 1/96 of an Imperial pint). The transition period during this switch-over will require careful watching by practitioners. Otherwise, as the *Pharmaceutical Journal* points out, "we might have to write labels to read 'Two teaspoonsful (medicinal) to be taken, etc.' ".

Industrial Welfare Society

ONE of Mr. Lloyd George's happiest appointments was that of Mr. Seebohm Rowntree, in 1915, to the charge of the special department just set up in the Ministry of Munitions to look after the welfare of munition workers. To assist him in his work Mr. Rowntree "borrowed", from the Bishop of London, the Rev. Robert Hyde, the vicar of St. Mary's, Hoxton. As a result of this collaboration was born the Industrial Welfare Society, which during the last thirty years has played such a vital part in establishing mutual understanding between employees and employers throughout industry in this country. An important milestone in the history of the Society has recently been reached in the opening of a new home for the Society in Bryanston Square, London, by Mr. Seebohm Rowntree who, in his eightieth year, can look back upon a lifetime of devoted service to an aspect of social science which he has made peculiarly his own. The new headquarters has been named "Robert Hyde House", thus perpetuating the great work of Sir Robert Hyde, as he now is, the other partner in this important task of humanizing industry.

The Practitioner under the Microscope

DR. JOSEPH COLLINGS is an Australian from Sydney who has been given a grant by the Nuffield Trustees to conduct an inquiry into general practice in England. His report appeared in the *Lancet* of March 25. As a record of hard work it is impressive. As evidence of the ability to sort evidence, to assign to statements their relative weight, and to draw conclusions having a significant value, it is disappointing. That such an inquiry should be undertaken at the present time is probably right. That the result should have been published as it stands is unfortunate. The place for such a document is a confidential report to the Nuffield Trustees who, after discussing its implications with the Ministry of Health, might have made it the basis of a valuable and helpful memorandum. The recommendations are constructive and contain much of value. In this context a practitioner writes to us:—"I do feel that urgent consideration should be given to keeping the G.P. in contact with hospitals. General practice will

always remain an art that will not be confounded by the multiplying methods of scientific medicine, but the perspective of the practitioner will only remain true if he is kept in contact with changing medical thought. Hospitals might well establish attached clinical societies where the general practitioner could demonstrate his own cases to his colleagues and in the presence of consultants".

The Doctor as Executioner

THE recent acquittal of an American doctor on the charge of "mercy killing" has raised once again the subject of euthanasia. The sanctity of human life is a fundamental Christian belief but one that the majority would interpret in the words of Clough: "Thou shalt not kill; but need'st not strive officiously to keep alive". All illnesses are not necessarily fatal. All fatal illnesses are not necessarily painful. But some diseases, notably cancer that has spread widely and become resistant to all forms of therapy, progress surely yet slowly to an agonizing and intolerable end. When faced with a patient so afflicted most practitioners would feel it their duty to ensure that his remaining days were as happy as possible, and would prescribe drugs like morphine and cocaine in doses that they would hesitate to give to one who had a chance of recovery. They might feel that the sufferer had the right to demand to be released from an existence so intolerable; even that his relatives might request that he should be helped to die. But they could never agree to the responsibility of making the decision themselves, or of administering the quietus at the request of the sufferer or his family. To deviate from this attitude would be to open the door to every form of criminality and crooked dealing. If euthanasia is ever to be legally permitted, the decision as to when in the course of any illness it is permissible must be made by some entirely disinterested and legally constituted Tribunal.

The Urge to Purge

ALTHOUGH, as was emphasized in Mr. Kinsella's outspoken article in our April issue (p. 333), the urge to purge dies hard, it is comforting to be reminded that in this respect at least, we have made some progress during the last hundred years or so. Whilst the writings of the physicians of a century ago are full of shrewd clinical observations, much of their therapeutic wisdom has rightly been cast into the limbo of the archaic. It may well have been a heroic age, but even making every allowance for their ignorance of physiology and pharmacology, it is difficult to understand how such able men, as many of these old physicians undoubtedly were, could possibly recommend the excessive purgation to which they submitted their unfortunate patients. Even Royalty did not escape, and the following extract from one of the famous Creevey letters, describing the treatment to which Queen Caroline was submitted in her final illness in 1821, makes one realize that there were disadvantages in living in those "good old days":—

"As to his Royal Mistress, his account was most curious. On Friday last

she lost sixty-four ounces of blood; took first of all 15 grains of calomel, which they think she threw up again in the whole or in part; and then she took 40 grains more of calomel which she kept entirely in her stomach; add to this a quantity of castor oil that would have turned the stomach of a horse. Nevertheless, on Friday night the inflammation had subsided, tho' not the obstruction on her liver".

The Little Busy Bee

To many of us honey is—well—just honey; either a delicacy beloved by our children or a subject of endless discussion by our apiarist friends. Those of our readers who belong to this school of thought will be well advised to read an article in the *Indian Medical Gazette* (October 1949, p. 446) in which the "commercial and therapeutic value of by-products of bee farming industry in India" is discussed with a mass of fascinating data. These by-products consist of royal jelly, bee venom, bee glue, beeswax, and pollens. Royal jelly fully deserves its alternative title of bee milk as it is similar in composition to human milk, although containing more protein and carbohydrate. It contains as much vitamin B as whole wheat and, in addition, is bacteriostatic to certain gram-positive organisms such as *Staphylococcus aureus*, and contains gonadotrophic hormones. Bee venom, which contains a neurotoxin, a hæmolysin and an endotheliotoxin, is said to be of value in the treatment of rheumatism. Bee glue, which is obtained by the worker bees from the resinous exudates of buds of various trees such as the balsams, conifers and poplars, and is used to seal the outlet of the cells of the hive, is used by indigenous practitioners in India as a local application "in order to ripen the deep abscesses and chronic ulcers". The uses of beeswax are summarized as: "It has been used for a long time in making candles and as earplugs to deafen noises. It is now used in paints, polishes, pillmass, plasters and ointment and in various other products of industries". Of the therapeutic and nutritive merits of honey itself, with its rich content of dextrose, lævulose, riboflavine, calcium, iron and copper, space forbids a detailed review, but it is interesting to note the emphasis laid upon the value of honey as a food for infants, children and invalids.

To our American friends, however, with their annual output in the region of 169,000,000 lb., honey has an infinite variety, as is shown by the following quotation from the *American Bulletin of Honey;* "About 6,000,000 lb. of honey is used in different types of cookies, in making bread, beverages, cakes, candies, fruit drops, sauces, meats and fish preparations; pies, puddings, salads and other vegetable preparations. Honey is used in golf-balls to make them heavy and of the proper specific gravity. Honey is added to the chewing tobacco, chewing gums, cigarettes and babies' sucking teats. The smoking pipes are immersed in honey for some days to cure them. It is added to cosmetics, tooth-pastes and shaving creams. It is used to enhance the natural darkness of onyx and other stones used in jewellery. It is also used in weather-proofing of leather".

OCCUPATIONAL DERMATOSES

By GODFREY BAMBER, M.D., F.R.C.P.

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THE skin, having as one of its functions that of protecting the parts beneath, has to, and in fact does, withstand fairly well the ordinary contacts of life. In the present age, however, when both in industry and the home there is an increasing use of substances elaborated by the chemist, the skin has to withstand new and greater strains to which it has not been biologically accustomed, so that, not unnaturally, it breaks down at times. Thus the face of dermatological practice has changed over the years, and the newer aspect has its legal bearings through Acts of Parliament devised to protect the worker in industry. In this connexion it is natural to think first of dermatitis because it is the most common of the industrial dermatoses, but infections must not be overlooked. Anthrax still occurs in those who handle hides and wool, although, thanks to the newer therapeutic measures, it is not so serious to the patient as it used to be. Other occupational infections are erysipeloid in those who handle meat and fish; primary skin tuberculosis and a host of other diseases that may be transmitted from animals to the farm worker and the veterinary surgeon; cowpox, contagious pustular dermatosis, actinomycosis, ringworm. Yeast-like fungi attack the skin of confectioners and workers in sugar. After long-continued exposure to certain irritants, such as tar and ultra-violet light, the skin shows degenerative changes which may eventually become malignant. Rarely, epitheliomas may develop rapidly on tar burns, and I have seen several young men with scrotal epithelioma who had worked on low temperature carbonization retorts for less than three years.

INDUSTRIAL DERMATITIS

Industrial dermatitis was defined for the purpose of the Workman's Compensation Act as dermatitis produced by dust or liquids with which the worker came into contact in his occupation. To some medical men the term dermatitis is synonymous with that of eczema, but for the purpose of the Act it had the wider and more literal meaning of inflammation of the skin. The late-developing epitheliomas in oil, pitch and tar workers were scheduled separately.

Broadly speaking there are two main types of occupational dermatitis: first, when there is a direct chemical, thermal or mechanical irritation of the skin, and secondly, when contact with a substance does not cause any obvious irritation for a time but after a short or longer period there is an excessive reaction to subsequent contacts, because the skin has become supersensitive to it. The rash is often not restricted to the sites of contact with the sensitizing agent, because the reaction is an allergic one and the whole of the skin may have become sensitized. Occasionally, but not

commonly, irritants of the first type may also sensitize the skin.

The first type of reaction usually occurs with corrosives such as strong acids, alkalis and other noxious chemicals. In occupations where these are regularly handled it is customary to wear protective clothing and to take other precautionary measures to diminish the chances of injury. When new manufacturing processes are introduced there is often a high incidence of dermatitis until the hazards have been accurately assessed and guarded against.

Clinical features.—The clinical appearance of the lesions in this first type vary considerably. Rarely, there may be necrosis of the skin followed by ulceration which may heal fairly quickly or run an indolent course, as happens in lesions from chromates. Keloids are more liable to develop in the scars of acid burns than in those of a different origin. More commonly, particularly on the hands which are, generally speaking, the parts most exposed to injury, there is an acute erythema thickly studded with vesicles and bullæ, rapidly followed by a considerable degree of œdema on the back of the hand. Secondary infection of the blisters by organisms already on the skin is usual, and there is increased pain and tenderness, with perhaps obvious lymphangitis and regional adenitis. It is not generally realized that there is a constant circulation of lymph into the skin which is drained away through the lymphatics, and that the rate of this circulation is much accelerated by trauma which increases permeation and dilates the lymph vessels.

The usual reaction, especially when the rate of irritation is slower, is an eczematous one, that is, the development of minute vesicles or vesicopapules on an erythematous background. This type of eruption is, of course, not restricted to occupational dermatitis. It is one of the most common responses of the skin to many kinds of irritant both external and internal, and its aspect varies with the stage at which it is seen. Sometimes, only the follicular part of the skin is affected by the injurious agent, which may be dust or one that easily mixes with, or is soluble in, sebum and so readily penetrates the follicle. Oils, especially cutting oils and emulsions used in engineering, chlorinated naphthalenes and some tars are typical examples of this class. The skin reacts to mild irritation of this kind by a thickening of the epidermis around the mouth of the follicle, so forming acneiform papules with a black comedo-like centre and occasionally a little roughening of the epidermis. The distribution is usually much wider than that of acne vulgaris. This early stage is so common on the limbs of those in oily occupations as to be disregarded. Incapacity only begins with the further evolution of the papule as an obvious inflammatory reaction in the upper part of the follicle, followed by pustulation of varied severity.

Rarer forms of reaction affect only certain functions of the skin, e.g. pigmentation. Pitch and tar in the early stage may lead to excessive pigmentation, whilst depigmentation and leuconychia are sometimes seen in the rubber industry and workers in brine.

The second main type of reaction is often indistinguishable clinically from allergic manifestations due to other causes and so makes diagnosis more difficult.

DIAGNOSIS

Before assuming that a dermatosis is probably an occupational one the following points must be determined satisfactorily.

(1) Is the patient's work known to cause dermatoses, or has he been in contact with any injurious agent?

(2) Does his type of rash fit in with the facts known about that particular dermatosis?

(3) Did the rash begin at the site of greatest exposure, and is it worse there than elsewhere on the body? This important proviso may be invalidated if the patient has had a rash on a previous occasion.

(4) Was the patient in contact with the alleged irritant shortly before the rash occurred? A long interval between the last contact and the outbreak of an eruption would invalidate most claims. The late developing keratoses and epitheliomas in pitch and tar workers are notable exceptions.

The natural history of the rash when known is usually helpful. If the rash improves rapidly when the patient ceases work, recurs when he returns to work after the skin has healed, then an occupational origin is likely. The case history should always be obtained as accurately as possible, but it should be remembered that the patient's thought is *post hoc ergo propter hoc*, and this colours his account. Occasionally he deliberately tries to mislead.

Patch testing.—Is it possible to confirm or refute a supposition that a particular substance is the probable cause of the rash? Assuming that the skin generally has become sensitized to an irritant, it should react to any subsequent contact with this substance even in an apparently healthy area. The strength of the test application should not be so great as to cause a primary irritation, and preferably should be too weak to cause a flare-up at the original site of injury. This is the basis of the patch test, in which the substance to be tested is applied to sound skin in a dilution that is too low to make a normal unsensitized person react (tables of concentrations for most of the substances used in industry are available for reference, e.g., in Bettley's "Skin Diseases in General Practice", 1949, p. 242) and left in contact for twenty-four hours and any reaction then noted. Should there be none, the site ought to be inspected daily for a week on the chance that the reaction is a delayed one. If the patch irritates the skin before the expiration of the twenty-four hours it must be removed immediately. Control tests with other substances are made at the same time.

A positive reaction should be interpreted cautiously; it may be a non-specific one in a subject with allergic tendencies or arise from some error in technique. An absence of reaction does not necessarily exculpate the substance tested, because its sensitizing power may be low and only the skin at and close around the site of injury may be supersensitive: this applies

particularly to the early stage of a sensitization dermatitis. Or the skin may be in an anergic phase. A test with the actual cause of the rash will give a negative reading if it has been tested the wrong way: for example, bakers sometimes become sensitive to ammonium persulphate, an improver in flour, and sometimes to flour itself. Their epidermis becomes sensitized to the former through handling dough, and a contact patch test is likely to be positive. Flour sensitizes them by inhalation, so a patch test will be negative; a percutaneous test is necessary to bring the flour into contact with the deeper layers of the skin, and the reaction is urticarial rather than eczematous. Some boys in a trade school were patch tested with ammonium persulphate. Two of them with positive patch tests who had become bakers, despite attempts to dissuade them, were still free from skin trouble at the end of two years. Patch tests are not for casual use; they should be made and interpreted by an expert.

CONTRIBUTORY OR CAUSAL FACTORS

Why is it that in many occupations only a small fraction of those engaged in it ever get dermatitis? Undoubtedly some people are more prone than others to develop rashes: they may have an allergic diathesis. Carelessness or ignorance on the part of some of them may be a cause.

A young french polisher told me that he cleaned his hands with strong soda. When warned of the dangers of this method he replied "Why should I worry? If they go wrong it will be worth sixty quid to me".

When the skin becomes soiled at work it is not infrequently cleaned with petrol, paraffin, alkalis and other solvents which remove the natural grease on and in the skin, so making it more vulnerable to several kinds of irritant. Very often a dermatitis is due to cleansing alkalis and not to the alleged irritant, which is harmless though unsightly. The married woman in industry has become a problem. Is her rash due to substances encountered while at work, or is it due to the alkalis she uses for cleaning her hands afterwards? If the latter, what proportion of the damage is attributable to this and what to the cleansers of various kinds used in the home? Is her occupational dermatitis that of an employee or that of a housewife? Although she has ceased to go out to work, does her rash persist because she is still carrying on a hazardous occupation at home? The risks run in cleansing are well illustrated in the mining industry. Miners are now often incapacitated by ringworm infection of the feet. This is a comparatively recent affection among them, one that has become prevalent since the general installation of pithead baths. The infection is caught not while they are working but afterwards, in the changing rooms.

The length of time the patient has worked at his particular trade does in some occupations determine the onset of a rash. When beginning many kinds of work for the first time there is an extra strain thrown on the skin to which it reacts mildly without necessitating time off, and then it becomes accustomed to the new conditions. Occasionally this mild reaction gets

worse because no hardening or immunity has developed. On the other hand, it may be many years before a baker becomes sensitive to flour or improver. This long delay in acquiring sensitization or losing tolerance suggests that there are other factors which determine the onset of the rash.

The age of the patient cannot be neglected. With increasing age the skin, like the rest of the body, degenerates and cannot withstand irritants so easily as it used to. Quite apart from work the incidence of eczema rises with advancing years and its appearance may be confused with an occupational eczematous reaction.

In case histories it is commonly found that the onset of occupational dermatitis has been preceded by a severe cold or similar illness that has been somewhat neglected by the patient, or by a period of domestic stress or anxiety. Less frequent is an onset after a holiday.

PROGNOSIS

With adequate treatment and absence from work until the skin has healed again, the great majority of patients suffering from occupational dermatitis recover completely and suffer from no disability later. Most of the remainder also recover quickly, but they may break down again at some subsequent encounter with the irritant because they have become to some degree sensitized. Occasionally the skin heals but readily breaks down again, not only on contact with the original irritant, but also with others of a widely different type. This seems to depend upon the nature of the original injury, which apparently impairs the vitality of the skin permanently. Burns from mustard gas and some other substances of that kind seem the most likely to end in this manner. When the rash is an allergic manifestation recurrence is likely on subsequent contact with the sensitizing substance but not with other unrelated compounds.

The *attitude of the patient* towards his condition undoubtedly influences its progress. Not infrequently when first seen he asks "Is it dermatitis, Doctor?" in the tones of one dreading an affirmative answer to the possibility of leprosy, plague or life-long invalidism. The Workman's Compensation Act, although on the whole an undoubted boon to the employee, encouraged the indolent and the malingerer and abetted the morbid interest of the introspective in their progress or lack of it. Some felt themselves to be victims of social injustice and sought recompense for their injured feelings and skin; they developed a compensation neurosis. Others find the disability a convenient peg on which to hang psychological problems connected with work or with private life. Younger people may dislike their work or have difficulty in getting on with those in charge of them. In the elderly there is sometimes the fear of being no longer able to do their job efficiently. Talking of psychological treatment Gillespie said "to give psychotherapy successfully to a workman who knows that if he gives up his symptoms he also gives up a safe 30s. a week for an uncertain future is a far harder and virtually an impossible task". Although the new Health Act has replaced

the Workman's Compensation Act, the old attitude to industrial disability is, in this age of safety first and social security, likely to persist for a long time.

TREATMENT

First-aid treatment to neutralize acids, alkalis and the like, on the skin should be given when necessary; otherwise infection, ulcers and dermatitis should be treated in the same manner as those of non-industrial origin. The industrial aspect should not, as a rule, be stressed to the patient; but every effort to restore the skin to normal as soon as possible should be made by forbidding the patient to carry on with his work, however trivial the rash may appear, and ensuring that his skin is protected from other possible irritants which might aggravate the condition; and, if the skin does not respond quickly to his practitioner's treatment, further advice should be sought without delay. A weekly visit to a surgery for a certificate and "*rep. ung.*" should be stopped. Incredible as it may seem, there are patients with industrial dermatitis who have drawn disability pay for months without ever being referred to a dermatologist for treatment. Industrial dermatoses cause more economic loss than do industrial accidents: for the latter, fracture clinics are considered to be necessary.

PROPHYLAXIS

In the dangerous trades special precautions are taken and are usually adequate. In many works technical modification of plant could be made to diminish splashing, improve ventilation, and so on. Protective overalls are useful but often make the wearer uncomfortably hot. Not infrequently working clothes are saturated with oil, and I have seen workers on gas retorts whose trousers were stiff with tar. It is possible to get clothing that is waterproof, fireproof or windproof, and it should not be beyond the ingenuity of the textile manufacturers to produce materials that are impervious to deleterious substances.

For the protection of the skin itself there are *barrier creams*. No cream is efficient for all purposes, it should be designed for the particular task it has to do, e.g., keeping out oil or water, buffering acids, alkalis, and the like. No external safeguards will eliminate occupational dermatoses; the workman must be educated or drilled into treating his skin with respect.

It may be advisable to examine the skin before the prospective employee takes up certain kinds of work. Those with seborrhœic skins are more prone to develop oil acne, and abnormally dry skins are unsuitable for occupations that entail contact with alkalis or where much washing is needed to keep the skin clean. The constitutionally allergic are quite unsuitable for many jobs, and the ordinary varicose eczema may spread from the leg to the hands, irrespective of the work done.

MEDICAL HAZARDS OF BERYLLIUM

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BERYLLIUM was discovered in 1797 by Vauquelin, who called it glucinium, owing to the sweet taste of its salts. It is a brittle, steel-grey metal with A.W. 9.02, S.G. 1.85 at 20° C. and M.P. 1300° C. It belongs to the calcium, magnesium and barium group in the periodic system of elements. It is soluble in acids and occurs chiefly as beryl, the double silicate of beryllium and aluminium (Be_3Al_2 (SiO_3)6). The clear crystals of beryl are perhaps better known as emeralds and aquamarines. Phenacite (Be_2SiO_4) and chrysoberyl ($Be_2Si_2O_4$) also occur.

Beryllium has certain properties important in industry. A small percentage added to copper forms an alloy with high electrical conductivity, increase in tensile strength and resistance to corrosion; a most useful alloy for aircraft, springs and non-sparking tools. In combination with silica, zinc and manganese, it also forms a fluorescent powder. Among the industrial uses of beryllium are alloys, fluorescent lamps, incandescent lamps, neon sign tubing, gas mantles, X-ray windows, radio tubes, electric heating elements, phosphor compounds, vitreous enamels, textile fibres, and chemical, pharmaceutical and atomic energy products.

Before the last great war beryllium was little used, but in the period of armament expansion the production of beryllium was greatly increased. Now, since the war, it is being used extensively in the expanded industries dealing with fluorescent lighting.

TOXICITY

Beryllium was first blamed for causing illness by Zamakhovskaya, and Martinkovsky and Syroechkovsky, in 1934, and it was not until nine years later that van Ordstrand *et al.* (1943) in America, reporting on three cases of chemical pneumonia, again drew attention to the rôle of beryllium as an industrial hazard. Since then considerable attention has been focused on the toxicity of beryllium, and several clear-cut clinical conditions have been recognized. Cases have been reported from this country (Agate, 1948; Royston, 1949), and from France (Roche, 1950), but although it is used in Belgium, Sweden and Holland no cases from there have yet been reported.

In the earlier days doubt was cast on the toxicity of beryllium *per se*, but the present view is well expressed by Tabershaw (1949) who says: "Beryllium and its salts are toxic and produce in man acute pulmonary, chronic pulmonary, dermal and systemic manifestations. There is abundant epidemiologic, clinical, pathologic and experimental evidence to support the thesis that the beryllium ion is toxic to man".

It is perhaps well at this stage to mention briefly the evidence on which beryllium has been incriminated. Experimentally, Aldridge *et al.* (1949)

have shown that the lethal dose of beryllium for rabbits, rats and mice is 0.5 mg. to 1.0 mg. of a solution of an ionized salt given into a vein. Death occurs in one to three days from liver necrosis, and they do not consider it to be due to the anionic component or acidity. Injection into tissues or inhalation both caused inflammatory changes. Further evidence that the ionic component is to blame is furnished by Aub and Grier (1949), who reported cases in laboratory workers who had been in contact with practically pure beryllium as the element or its oxide. They had not been in contact with any other beryllium salts. Campbell *et al.* (1942) showed that an alloy containing nickel, cobalt, chromium and molybdenum did not cause any tissue reaction, but the addition of 1.6 per cent. beryllium to this alloy caused the formation of a chronically inflamed granulation tissue containing many macrophages.

NASOPHARYNGITIS, TRACHEO-BRONCHITIS AND ACUTE PNEUMONITIS

There appear to be two main types of respiratory disease, the acute and the delayed, but although these are often clinically distinct they are not so pathologically, and Dutra (1948) considers that all gradations between acute and chronic probably occur, this possibly being due to the varying degree of solubility of the compound at fault. No acute case has yet been reported as progressing to the chronic stage, which is rather surprising if Dutra's view is correct.

Nasopharyngitis and *tracheo-bronchitis* result from exposure to fumes and invariably precede pneumonitis but often occur independently. If the exposure is sufficiently severe the symptoms may come on within a few minutes, but in the concentrations commonly met with symptoms do not usually occur for a few days. Irritation of the eyes and nose with tightness felt across the front of the chest and a dry hacking cough that may resemble whooping-cough are the chief complaints. They clear up promptly when the exposure ceases.

Acute pneumonia.—This may be fulminating and occur within a few hours of exposure, but more commonly has an insidious onset some weeks or months later but while the subject is still exposed to beryllium. In this way it differs from the delayed pneumonitis or chronic pulmonary granulomatosis, as it is now called, which comes on some time after exposure to beryllium has ceased. The chief symptom is exertion dyspnœa, which is usually associated with weakness, an unproductive cough, some tightness in the chest and mild malaise. The respiratory rate is often raised and may be markedly so. Fever is not characteristic but the pulse rate is increased. The dyspnœa is out of all proportion to the physical signs, which are usually limited to a few scattered râles accompanied in the more severe cases by cyanosis. The vital capacity is decreased to as low as 40 per cent. of normal. A certain amount of bronchial spasm is common. Cyanosis may be severe.

The *X-ray appearances* are interesting and have been well described by

Wilson (1948), who recognizes three stages. Stage I, a fine diffuse granularity which under a reading glass resembles a sand-storm effect. There is no increase in the linear markings. Stage II, the addition of a diffuse reticular pattern to the appearances in stage I. Stage III, the appearance of distinct nodules, from 1.5 mm. to 2 mm. in diameter, evenly distributed throughout the lung fields, in addition to the previous changes. He considers that the appearances in stage I are pathognomonic of beryllium. If the patient recovers, the X-ray appearances gradually regress and become normal. There is no residual fibrosis. These changes may precede the symptoms and usually outlast them, but exceptions to this are common.

Laboratory investigations are unremarkable. Evidence of tuberculosis or syphilis has not been found. The erythrocyte sedimentation rate is only slightly increased and the blood chemistry is normal. There is sometimes mild polycythæmia and some increase in the haemoglobin level. Albuminuria has been reported.

Dutra (1948) described the gross tissue findings at autopsy. The lungs were heavy and had lost their elasticity. The cut surfaces were homogeneous and a moderate quantity of thin fluid could be expressed. The pulmonary and peritracheal glands were soft, fleshy and moderately enlarged. The histology revealed a mononuclear exudate and the early formation of new connective tissue. For a more detailed account the reader is referred to the original article. Apart from the lungs the other viscera were normal, except for hepatic centrilobular necrosis in one case which also showed several areas of coagulation necrosis of the vertebral bone marrow.

Treatment.—This is symptomatic. Oxygen therapy may be needed in the more severe cases. The sulphonamides and the antibiotics are useless. The antihistamines have been found useful by some workers but probably do not affect the course of the disease. Prognosis is quite good but will depend upon the degree of exposure and the individual sensitivity of the patient. The mortality is probably less than 1 per cent.

CHRONIC PULMONARY GRANULOMATOSIS

At the Sixth Saranac Conference held in 1947, a subcommittee was formed to advise on the nomenclature of beryllium diseases. It recommended that the chronic form of beryllium pneumonitis should be called chronic pulmonary granulomatosis of beryllium workers instead of delayed pneumonitis as hitherto, and that the acute form should be known as acute pneumonitis of beryllium workers.

The chronic condition is characterized by delayed onset, and symptoms may not occur for six months to six years after cessation of exposure to beryllium. Hardy and Tabershaw (1946) reported 17 cases. Four of these developed while the workers were still exposed to beryllium after periods of exposure varying from three months to five years. The remaining 13 developed symptoms from three months to three years after cessation of exposure. Agate's case (1948) had not been in significant contact with

beryllium for three years and Wilson's case (1948) for six years.

"Neighbourhood cases" have also been described (Hunter, 1950; Tabershaw, 1949). These occur in people who live in the vicinity of factories engaged in beryllium production. In some cases it has been shown that the beryllium has been introduced to the home on the clothes of workers from the factory, thereby causing illness in contacts, but in some instances no form of contact with the factory could be established, and in these cases atmospheric pollution has been blamed. Hunter (1950) quotes atmospheric concentrations three-quarters of a mile from a factory, ranging from 0.01 μg. to 0.1 μg. per cubic metre, but it has not yet been established at what atmospheric concentration beryllium is hazardous.

The *symptoms* are much the same as for acute pneumonitis but, in addition, weight loss is marked and accompanied by anorexia. A nasty taste in the mouth may also be present. Dyspnœa is very prominent, together with fatigue. Hæmoptysis has been reported. Diminished vital capacity, orthopnœa with raised respiratory and pulse rates and scattered sibilant râles are the most common signs. Cyanosis is present in severe cases, together with emaciation. Fever is usually low-grade unless secondary infection sets in, but this is uncommon except in the later stages. An electrocardiogram may show hypertrophy of the right side of the heart.

X-ray appearances.—These do not differ from those already described under acute pneumonitis. A miliary appearance may occur in either the acute or the chronic form of the disease. The radiological differential diagnosis may be difficult, and Pascucci (1948) considers that uncomplicated silicosis is indistinguishable from the nodular stage of beryllium granulomatosis. Miliary tuberculosis shows the nodules but does not show the finely granular background of the beryllium condition. Virus pneumonitis, erythema nodosum (Kerley, 1942), Bœck's sarcoid, the pulmonary mycoses, generalized carcinomatosis, the pulmonary appearances in radiator and boiler finishers who inhale a dust containing carbon, iron and silica (Dunner *et al.*, 1945), chronic welders' disease and workers with tremolite talc powder (Siegal *et al.*, 1943) may all require differentiating from beryllium conditions.

Pathology.—The gross morphological findings (Dutra, 1948) consist of heavy lungs, usually ranging between 1500 and 2000 g., and in one case 2400 g. Elasticity is lost, but unlike the acute pneumonitis the cut surface is not homogeneous, but contains many firm nodules up to 2 mm. in diameter. Emphysema is invariably present; although usually scattered it may be localized. This mixture of nodules and emphysema sometimes gives a generalized honeycomb appearance. The related lymph glands are usually firm and enlarged. Cardiac changes are commonly present in the form of dilatation of the right ventricle with hypertrophy of the muscle. Histologically there is marked fibrosis with emphysema and granulomas. Agate (1948) described focal granulomas in the liver in material obtained by drill biopsy.

Complications.—Chronic cor pulmonale has been frequently noted and may be the cause of death. Secondary infection may occur, but is late rather than early.

Prognosis.—Chronic pulmonary granulomatosis is usually a severe illness of long duration, and in 36 cases described by Hardy (1948), and followed up for from two to seven years, six had died, twelve were completely disabled, eleven were disabled, three were working and four were asymptomatic. The latter four had been discovered by routine X-rays and had always been symptom-free. The mortality is probably in the region of 10 per cent.

Diagnosis.—The diagnosis depends upon establishing some degree of past or present contact with beryllium and bearing in mind the possibility of the beryllium diseases when confronted with an obscure pneumonitis or miliary X-ray appearances that do not appear to fit clinically with miliary tuberculosis. The estimation of beryllium in the urine may be useful in non-occupational cases but is at present not generally available (Dutra *et al.*, 1949). Beryllium can also be demonstrated in autopsy material by special techniques (Aldridge *et al.*, 1949). Acute pneumonitis has to be differentiated from acute bronchiolitis and miliary tuberculosis.

Treatment.—No specific treatment has as yet been discovered. Oxygen is useful in the presence of cyanosis, and the antihistamine drugs may help bronchial spasm. The antibiotics should be given for secondary infection.

DERMATOLOGICAL MANIFESTATIONS

Contact dermatitis.—Beryllium affects the skin in two main ways. In the first place there is a contact dermatitis from the soluble salts, which is characterized by an œdematous papulo-vesicular eruption chiefly over exposed surfaces. It is accompanied by considerable pruritus and there may be weeping (Dunn and Pratt, 1949). The element of individual hypersensitivity undoubtedly influences the time of appearance and the extent of the dermatitis. About 25 per cent. of new employees have been found to be sensitive within three to ten days of exposure (De Nardi *et al.*, 1949). The antihistamine drugs have been tried with some success.

Ulceration.—The second type of skin lesion is the beryllium ulcer or granuloma. This is due to the implantation of a crystal of a beryllium salt into or under the skin. The most common way for this to occur is from the breaking of strip lighting tubes, when small fragments of glass, coated with a phosphor, penetrate the skin. The resulting lesion either fails to heal or a scar similar in appearance to a keloid forms and later breaks down (Dutra, 1949; Marshall, 1949; Nichol and Domingnez, 1949; Dunn and Pratt, 1949). The lesion consists histologically of granulomas of sarcoid type. These granulomas are both simple and conglomerate. The larger ones are surrounded by concentric collagenous fibres, and in the centres of many are pale areas consisting of coarse hyaline fibres. The main cellular elements resemble epithelioid cells. Lymphocytes and multinucleated giant cells of Langhans type are also present.

A similar type of skin lesion is that which may accompany chronic pulmonary granulomatosis. These have been described on the dorsum of the hand (Pascucci, 1948), and histologically showed sarcoid-like lesions indistinguishable from those appearing in the lungs. Marshall (1949) rightly warns against the danger to children of discarded strip-lighting tubes, and urges disposal and destruction under carefully controlled conditions. Treatment is excision of the lesion, which is always followed by healing by first intention.

PREVENTIVE MEASURES

Clearly, whenever possible, harmless substitutes for beryllium should be used. Considerable success in this direction has been achieved in the fluorescent lamp industry in this country by the introduction of halophosphates which contain no beryllium. When beryllium must be used, as in certain alloys, much has been done to diminish the hazard of inhalation and direct contact. Such measures include exhaust ventilation and the wearing of masks by operatives. Protective clothing has been made available and clean overalls should be issued daily. Both these latter should be discarded before meals. Adequate washing facilities should be provided before meals and at the end of the shift. Regular medical examinations with periodic chest X-ray examinations also help to detect early cases, and it is probably wise to limit the choice of worker to those in whom there is no history of chronic respiratory infection. All preventive measures should be taken in the firm's time and under supervision. The worker should also receive instruction in the risks involved and in the methods of prevention. By this means cooperation between the workers and the management is likely to be greater. In Great Britain beryllium poisoning has been made subject to compensation.

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OCCUPATIONAL JAUNDICE AND ANÆMIA

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In considering jaundice or anæmia, or a combination of both disorders, as the consequence of exposure to occupational hazards, it is necessary to examine the potentiality for injury of a large number of toxic agents, both physical and chemical, and a wide variety in the nature and degree of their effects. These effects may also be greatly influenced by nutritional deficiencies in the individual. For full and normal hæmopoiesis, in the words of Sir Lionel Whitby (1949), "an overriding requirement is a properly functioning alimentary canal which will ensure adequate digestion and absorption of the essential requirements which are then presented to a healthy liver for storage and distribution". The circulating blood and the hæmopoietic tissues of the body may be regarded as forming what has been termed the "hæmaton" (Piney and Hamilton Paterson, 1943), which includes the "erythron" and the "leucon", and of this system the bone marrow is the most important organ. Upon its adequate function depends to a great extent the integrity of the whole mass of circulating cells. Any individual therefore who suffers from nutritional or idiopathic disturbance of bone-marrow function is especially liable to suffer from dyshæmopoiesis when exposed to toxic substances with a specific capacity for injuring the bone marrow.

With regard to chemical compounds especially, certain groups with similar chemical constitution and properties have a tendency to attack the same bodily organs and systems, but within these groups the individual members differ greatly in their relative strength of attack on the different systems. Among the aromatic hydrocarbons, for example, of which benzene is the prototype, the chief point of action is the hæmopoietic system, but no other member of the group, which includes xylene and toluene, has so powerful or characteristic an effect as benzene itself. Some of the nitro- and amino-derivatives of benzene, such as nitrobenzene and aniline, behave in an entirely different manner from their parent compounds, showing as their characteristic toxic property the capacity to form methæmoglobin, whilst one member of the group, trinitrotoluene, has the predominant effect of injuring the liver. The liver is the chief site of injury by the halogenated hydrocarbons, but here again, the degree of injury varies greatly among the individual compounds, tetrachlorethane being liable to cause acute yellow atrophy, whilst trichlorethylene has scarcely, if any, effect on the liver.

AGENTS PRODUCING JAUNDICE AS THEIR CHIEF TOXIC EFFECT

The definition of "toxic jaundice" as a notifiable disease is such that it can

be extended to cover a very wide field of toxic agents. In the Statutory Rules and Orders 1915, No. 1170, the provision is applied to "all cases of toxic jaundice occurring in a factory or workshop; that is, jaundice due to tetrachlorethane or nitro- or amido-derivatives of benzene or other poisonous substance". Tetrachlorethane may be taken as the prototype of the hepatotoxic agents belonging to the group of halogenated hydrocarbons.

The *halogenated*, or *chlorinated*, *hydrocarbons* are compounds formed by the substitution of chlorine for hydrogen atoms; the most important compounds from the industrial point of view are the liquid chlorinated derivatives of the methane, ethane and ethylene series, since among these are some of the most efficient solvents known—methylene chloride, carbon tetrachloride, tetrachlorethane, trichlorethylene, ethylene dichloride, and many others. All are narcotics, and many are hepatotoxins, and although the magnitude of each of these effects can be correlated to some extent with the type and degree of halogenation, the total toxicity can only be judged by deciding whether the criterion is to be that of death occurring shortly after narcotic concentrations or of "delayed" deaths due to injury to the liver. In the methane series, for example, the narcotic effect of chloroform (CCl_3) is greater than that of carbon tetrachloride (CCl_4) but liver injury is greater with carbon tetrachloride than with chloroform. In the ethane series, tetrachlorethane shows the greatest hepatotoxic activity; in the ethylene series dichlorethylene is the only one from which definite liver injury has been reported.

The two most important jaundice-producing solvents of this group are undoubtedly tetrachlorethane and carbon tetrachloride. Both may attack the kidneys also; in the case of acute carbon tetrachloride intoxication nephritis is often the predominant injury, whilst the liver injury caused by exposure to relatively lower concentrations is much more likely to recover than is the case with tetrachlorethane.

Tetrachlorethane, which as an aeroplane "dope" during the 1914-18 war proved so toxic that its use for this purpose was forbidden in many countries, is a powerful solvent and is still used to some extent in degreasing, paint removal, extraction of fats and, in France especially, in the manufacture of artificial pearls. Inhalation of large quantities may prove fatal from its acute narcotic effect before liver injury has become apparent, but its greatest hazard is the "delayed" metabolic effect from repeated non-narcotic concentrations. The maximum atmospheric concentration now regarded as safe for continued exposure is 10 parts per million.

Premonitory symptoms of poisoning are sometimes related to the nervous system, more often to the gastro-intestinal tract—loss of appetite, nausea, vomiting, abdominal pain. After an interval lasting from three days to three months, jaundice appears, progressing to the "toxæmic" stage, with enlarged and tender liver, delirium, convulsions and coma, leading to death with or without the stage of ascites and albuminuria. The jaundice is obstructive in nature, due to inflammation of the small intra-hepatic bile

ducts, followed by toxic fatty degeneration and necrosis (acute yellow atrophy).

The course and nature of *carbon tetrachloride* intoxication is somewhat different. Carbon tetrachloride is widely used as a solvent, cleaner and degreaser and as a constituent of many fire extinguishers. It was at one time regarded as the most toxic of all the halogenated hydrocarbons, but recent investigations tend to show that with proper safeguards against high concentrations its effects on the liver, although often unpleasant, are neither severe nor permanent. Most of the severe cases of poisoning reported have occurred when concentrations have been well above 100 parts per million, a level which it is entirely possible and practicable to reach in most of its industrial applications. With high concentrations, such as may arise when fire extinguishers are used in a closed space, in accidental inhalations from vessels containing carbon tetrachloride, or in badly regulated dry-cleaning establishments, the initial narcotic effect, although sometimes severe, may quickly disappear, but after an interval of three to twelve days, symptoms of involvement of the liver or kidneys, or both, arise. In the "hepato-renal" type of poisoning the predominant feature is usually jaundice; in the "pure renal" type, albuminuria, hæmaturia and anuria are the most conspicuous signs of injury.

With exposure to lower, repeated, concentrations, the liver is not likely to be severely or permanently injured, even though symptoms of gastro-intestinal disturbance may be serious enough to cause considerable ill-health. This is because the toxic effect is more functional than organic, and because regeneration of damaged liver cells takes place rapidly on cessation of exposure (Stewart and Witts, 1944).

Chlorinated naphthalenes.—Among the other "poisonous substances" which may cause jaundice are the chlorinated naphthalenes and phosphorus.

When naphthalene is chlorinated, a wax-like substance (chlorowax) is formed, which is used in industry as an insulating coat on electrical wires, or on metal to limit the action of plating processes. Inhalation, ingestion, or skin absorption of the dust or fume may produce, in addition to the characteristic skin lesion known as "chlor-acne", severe injury to the liver. In a fatal case described in the Annual Report of the Chief Inspector of Factories, 1942, jaundice first occurred about six months after exposure and death a month later; at autopsy the liver showed acute yellow atrophy.

Phosphorus, of which the yellow variety was once of great industrial importance and hazard in the match industry, has now been largely superseded by safer substitutes, although it is still used in the manufacture of phosphor bronze. The present infrequency of its most alarming manifestations, necrosis of the jaw ("phossy jaw") and intense jaundice, is another outstanding example of the control of toxic hazards in modern industry. Jaundice, accompanied by gastro-intestinal disturbance and loss of appetite, is an early sign of phosphorus poisoning, and the liver injury is believed to be due to inhibition of glycogen formation and of normal enzymic liver function, so

that while autolytic processes continue, toxic decomposition products are formed (Fischler, 1941).

AGENTS PRODUCING BOTH ANÆMIA AND JAUNDICE

Nitro- and amido-derivatives of benzene

These compounds, which include aniline, nitrobenzene, dinitrobenzene and trinitrotoluene, form a large group used in the dyeing industry, as accelerators and anti-oxidants in the rubber industry, and to some extent in paints, perfumes and fungicides. All have the characteristic property of forming methæmoglobin, and some, notably trinitrotoluene, of causing liver damage also. They are thus, as a group, agents which may cause both anæmia and jaundice.

Trinitrotoluene is another highly toxic substance which has shown itself amenable to control. In America, where vast quantities were used in the manufacture of explosives during the recent war, the number of deaths amounted to 22; a rate of only 3 fatalities per 100,000 operatives. Of these, 8 died of toxic hepatitis, 13 of aplastic anæmia, and one of a combination of both (Hamblin, 1949).

In the production of aplastic anæmia, trinitrotoluene is unique among this group of compounds, and its action on the liver, although more important toxicologically than its methæmoglobin-producing effect, is not of such frequent occurrence. "If cyanosis occurs in one in 10 of the workers, jaundice attacks one in 500" (Hunter, 1944). Jaundice may appear, however, several weeks after cessation of exposure, or sometimes without any premonitory symptoms. In fatal cases the liver shows yellow and red necrosis with little attempt at regeneration.

Nitrobenzene, or oil of mirbane, although it may produce jaundice, is pre-eminently a methæmoglobin-former, giving rise to the characteristic lilac cyanosis, and often to a very severe anæmia, but not of the aplastic type.

Dinitrobenzene also produces severe secondary anæmia, but jaundice is unusual.

Arsine (AsH_3), although producing jaundice, is primarily a hæmolytic agent, the liver function being disturbed more as a concomitant of disintegration of red cells than by actual disorder of the liver, although this may occur.

Exposure to arsine may occur in the process of cleaning metal tanks containing sulphuric acid, the hydrogen generated combining with arsenical impurities in the acid; also in the pickling and galvanizing of metals containing arsenic; in soldering, etching, and electrolysis of arsenious solutions, and in the reduction of nitro-bodies to amino-bodies. Its toxic action is first exerted on the red blood cells, where it combines with the hæmoglobin and causes hæmolysis with widespread destruction of the cells. Profound anæmia rapidly supervenes and the accompanying cyanosis, combined frequently with jaundice, gives the skin a characteristic bronze colour.

AGENTS PRODUCING ANÆMIA WITHOUT JAUNDICE

"Toxic anæmia" was made notifiable in 1942 (S.R. & O. No. 196), and its definition "is intended to apply to dyshæmopoietic anæmia occurring in a person employed in a process which brings him into contact with X-rays, radio-active substances and any chemical compound which may be capable of causing this effect".

It may be noted that under this definition cases of secondary or nutritional anæmia, probably having no association with occupational factors, may be included, since any variation of the normal blood picture may, in the widest sense, be regarded as "dyshæmopoiesis". From the point of view of diagnosing a true occupational anæmia this is of considerable advantage, since notification leads to further investigation of any such case, and its differential diagnosis from anæmia caused by the industrial noxious agent to which the person employed is exposed. It may also be noted that the term "toxic anæmia" gives an opportunity of notifying cases of anæmia due to exposure to benzene which could not, in the absence of "hæmorrhages under the skin and bleeding from the gums, nose and other passages in the last stages" be notified as "chronic benzene poisoning" (Factory Department, Home Office 1925, Form 1787).

The many toxic agents which produce dyshæmopoiesis may be classified as (1) those which act directly on the bone marrow; (2) those which act on the peripheral blood cells; and (3) those which form methæmoglobin.

Poisons acting on the bone marrow

(a) *Chemical substances.—Benzene* (C_6H_6), is the example *par excellence* of a substance which has a selective action on the hæmopoietic system. It is one of the aromatic hydrocarbons, to which group belong also its homologues, xylene and toluene and ethyl benzene. None of these inflicts the severe injury on the bone marrow characteristic of benzene, possibly because their metabolism within the body does not form the toxic oxidation products formed during the decomposition of benzene.

Benzene is one of the most efficient of all organic solvents and is therefore used extensively in a large number of industries: for extraction purposes, in organic synthesis, in the rubber and waterproof industries, as a thinner in paints and varnishes, in the manufacture of artificial leather, in cleaning and degreasing. In large doses it is a powerful narcotic, but its chief importance in industrial toxicology is its chronic effect in small repeated doses. The classical effect is that of aplastic anæmia, producing complete aplasia of the bone marrow, but this is by no means an invariable picture. The most frequent blood picture of severe anæmia with a high colour index, and leucopenia, is often complicated by the fact that the depressing effect on the bone marrow is accompanied by a regenerative activity, so that compensation may mask the destruction of both red and white cells. In some cases the initial effect is a hyper-stimulation with leucocytosis, whilst the final phase may develop into a fatal leukæmia. The experience of most workers in this

field of recent years, however, shows that the most reliable deviations from the normal blood picture in the early stages of "benzene absorption" are a fall in the total number of polymorphonuclear leucocytes, whether this be accompanied by a frank leucopenia or not, and a thrombocytopenia. The most unfortunate feature of chronic benzene poisoning is that symptoms do not go hand in hand with blood changes; it is often found that workers exposed to benzene do not complain of any disturbance of health except undue fatigue when their blood picture shows evidence of considerable damage to the blood-forming organs. It is unfortunate also, that removal from exposure, to be effective, must take place before the injury has gone too far; once the stage of hæmorrhage into the skin and mucous membranes is reached, no therapeutic measures seem to prevent a fatal outcome. A persistent effect has been noted by many observers; in my experience leucopenia has been found in some cases to remain unchanged for three or more years after all exposure has ceased, and in one case, in a woman who had been employed for four years in painting rubber rings with a benzene rubber solution, death took place after two years of non-exposure.

(b) *Radium and X-rays.*—Basically the anæmia which results from excessive exposure to the gamma radiation of radium or to X-rays is a manifestation of the lethal effect of ionization on the individual cell, its cytochemistry, its chromosome development and gene mutation.

In modern industry the use of radium and X-rays has two principal applications—the painting of dials and other instruments with "luminous compound" containing a small amount (5 to 70 micrograms per gramme) of radium salt, and the examination of castings and other articles by means of either the radium "bomb", a radon "seed", radioactive isotopes or X-rays. In all these industries such strict protective measures have been adopted that there is practically no possibility that exposure sufficient to cause a fatal anæmia could occur. Strict control of the actual dosage is now possible by the use of the Geiger counter or photographic films, and a result showing more than the maximum permissible dose, recommended by the British X-ray Protection Committee—0.5r per week—would call for close investigation of the process.

Over-exposure of any considerable degree is usually reflected in the blood picture as a depression of the polymorphonuclear leucocytes; sometimes a neutropenia only, sometimes a mild leucopenia, and since the lymphocyte is extremely sensitive both to the effect of excessive radiation and to recovery from it, the absolute lymphocyte figure may show great variations. Another pointer is the presence of abnormal cells in the stained film. These, in the form of primitive types of large mononuclear cells, have been observed most often in the stained films of the blood of luminizers (Browning, 1949).

Poisons acting on the peripheral blood

The principal example of a toxic substance acting, not on the bone marrow, but upon the cells circulating in the blood stream is *lead.* The mild

anæmia, accompanied by the presence of "stippled cells" or punctate basophilia, is regarded as evidence of lead absorption, prior to the development of the toxic manifestations constituting lead poisoning. Blood examinations of workers in lead processes, such as the manufacture of certain lead compounds, removal of lead-containing paints, as in ship breaking, the manufacture of electrical accumulators, and in many other industries where lead may be introduced into the body by inhalation of dust or fume or ingestion from contaminated food, are therefore of value, when combined with analyses of the atmosphere, blood, urine and fæces, in estimating the actual exposure. The significant findings are the presence of a low red cell count with a falling hæmoglobin level, giving rise to a colour index below 1, and of stippled erythrocytes above the level of 1000 per million red cells. Practically all workers exposed to lead show some punctate basophilia, which, of course, occurs in other forms of severe anæmia, but an abrupt progressive increase is strongly suggestive of lead absorption.

The anaemia is believed to be due to the actual precipitation of lead in the red cell envelope, making it more easily destructible, so that many red cells disappear from the circulation. This is followed by a compensatory regeneration with the appearance of immature forms, represented by the young stippled cells (Aub and Reznikoff, 1924).

Methæmoglobin producers

These have already been described under "nitro- and amido-derivatives of benzene".

CONCLUSION

It only remains to emphasize that the production of both anæmia and jaundice by some of these compounds points to the close relation of liver function and hæmopoiesis. In the words of Sir Lionel Whitby (1949): "The liver is recognized as the great site of detoxication and there is reason to believe that the primary action of most substances known to produce aplastic and hypoplastic blood conditions is to cause liver damage. Once the protective filter is eliminated the poison is free to act on the marrow".

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OCCUPATIONAL CARCINOGENESIS

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Not even the most sanguine would claim that the present state of knowledge on the fundamental cause or causes of non-occupational neoplastic disease is so far advanced that reasonable hope may be entertained of a curative or inhibitory chemotherapy or of a satisfactory preventive technique in the near future.

It is manifest that a great deal has been learnt in the last thirty years on the reaction of animal tissues and cells to a large number of synthetic chemical compounds and complex mixtures possessing carcinogenic properties. The imposing list of such compounds is rather a cause for depression than for hope, for the immense variety of structure of these materials seems almost to rule out any unitary hypothesis on how the effects are brought about. The chemical view of the etiology of cancer in man has naturally received great support from this work. Even the dilemma of the tumours induced in animals by virus does not present an insuperable barrier to the chemical view, for the time must come when the action of a virus will be expressible in terms of chemistry. It is the ancillary but vital character of a virus in the epidemiological field which might colour the picture, but the ultimate action on the cell must be of a chemical nature.

THEORIES OF CAUSATION

Whether it is a chemical compound as such or one produced by or incorporated in the structure of a virus, it is necessary for the carcinogenic agent to come into intimate contact with the cell which ultimately undergoes the change in character and rate of division which we call cancer. Various views are available as to what is the basic nature of such change, for example, that the enzymatic life of the cell is transformed; that the cell undergoes a type of mutation; that the normal processes of control or inhibition of growth are neutralized by carcinogens; that the cancerous transformation is really an adaptation of normal cells to adverse conditions created by the carcinogen; that the cancer cell arises from a slow breakdown of the activities of normal cells and not from a stimulus to its growth capacity, and no doubt many others. The common character of all such theories is that a point is reached in their exposition when experiment is left aside and imagination is allowed to enter.

The irreversible nature of the carcinogenic process which sometimes seems remarkable is perhaps not so surprising when the quite undisturbing irreversibility of tissue and organ differentiation from the primordial cell is borne in mind. The chemical nature of the so-called "organizers" which are apparently responsible for specific embryological differentiations seems well

established. There is probably a considerable specificity in the nature of organizers, bringing about definite effects. Such specificity does not, on the surface at any rate, appear to apply to carcinogens. Tumours can be induced experimentally in animals which are indistinguishable from tumours arising in man, both "spontaneously" and as a result of occupational absorption of the experimental carcinogen which is quite foreign to the metabolism of man.

EXPERIMENTAL EVIDENCE

The ultimate object in all cancer research is to prevent, inhibit or reverse the carcinogenic process. A great deal of experimental work has been done to attain this object in the case of experimental cancer. The skin cancer induced in mouse skin by the polycyclic hydrocarbons (e.g. 3:4-benzpyrene or 1,2,5,6-dibenzanthracene) and certain of their derivatives can be inhibited in different degrees by such widely differing substances as mustard gas and some of its derivatives, cantharidine, carbon dioxide snow, aliphatic aldehydes, and even strong sunlight. Even such unexpected compounds as naphthalene, anthracene and phenanthrene and bromobenzene were found to be inhibitory, and the fact that these compounds are excreted in animals in the form of mercapturic acid derivatives which arise from the condensation of a molecule of the compound and a molecule of the N-acetyl derivative of cysteine, led to speculation as to the importance in carcinogenesis of the deviation of sulphur from the normal metabolism of the skin cells. But even such anti-carcinogenic action in what must, compared with "spontaneous" cancer, be regarded as a relatively simple situation, is in no sense specific. Thus, certain skin-irritant compounds can act as co-carcinogens on mouse skin, but in appropriate dosage these can also act as anti-carcinogens, e.g. croton oil and croton resin; and the same applies to anti-carcinogens.

In all experimentation of this kind the inducer of the tumour and how it entered the body is known, the tissue affected is known, the nature of the tumour is known, and much of the relevant history of the animal is known. In human "spontaneous" tumours the nature of the tumour is, in general, known, the tissue affected is known, a little of the history of the animal is known, but of the inducer and how it entered, became active or was manufactured in the body, nothing is known.

In human occupational tumours a considerable amount is known about the inducer of the tumour as well as how it entered the body, in addition to the other elements referred to. It therefore follows that, just as in the experimental animal, the development of tumours can be prevented by not carrying out the experiment, so the occupational neoplasms need not develop if the "experiment" of exposing the worker to industrial carcinogens is not carried out.

SPONTANEOUS TUMOURS: PREDISPOSING FACTORS

Nothing is positively known, on the other hand, about how to prevent the "spontaneous" human tumours. Since tumours of this kind develop in

every class of human society, no absolute case can be made out for any obvious environmental factors, although statistical evidence may show a preponderance of certain forms of neoplasm in the poorer strata of society. It is probable that if a cross-section of society could be taken and wrapped in what might be called economic and physical cotton-wool, the incidence of tumours would in course of time be found to be quantitatively lower but qualitatively very similar to that found in normal conditions, i.e., there would be a cancer age-group, certain forms of tumours would be predominantly male or female in their sex incidence, and so on.

Genetic factors appear to enter in the appearance of "spontaneous" human tumours and there can be no doubt about them in certain animal strains. Attempts to demonstrate the weight of genetic character on the development of occupational tumours are not easy, in spite of the frequent presence of members of the same family tree in an industry with a carcinogenic hazard.

That *dietary factors* may enter as accessories in the etiology of human cancer has been considered in great detail but results have been inconclusive. Studies of records of American Insurance Companies led to the conclusion that there was a correlation between overweight and an increased liability to cancer. The same investigator, five years later, showed that both spontaneous and artificially induced tumours in mice can be delayed or even prevented when a carbohydrate-deficient diet was fed containing all the other recognized food constituents. Of course, such animals are stunted and there follows great endocrine atrophy. In this state the animals become refractory to the most active carcinogenic compounds. The recommendation by this investigator that diminished food intake should be practised as a prophylactic measure against cancer is perhaps a little naïve. When, as in the case of occupational tumours, the cause of the neoplastic process is known, no influence on the liability to develop the tumours which can be attributed to dietary habit has been discovered: such tumours develop in the well-nourished and in the relatively undernourished.

Age as a factor in the incidence of "spontaneous" tumours in man has for long been held to have a special significance, in spite of the apparent contradiction between the extreme vitality of a malignant process and the diminished vitality of the host body in which all passion appeared to be spent. Indeed, in some sense a cancer seems to be a process of local rejuvenation refusing to be bound by the general senescence. Age as a factor in occupational tumours is of secondary importance. Whilst it is true that occupational tumours often take many years to develop, the determinant as to the age at which they appear depends upon the age at which the tumour-inducing hazard was first met and how intensely the exposure continued.

CLINICAL AND PATHOLOGICAL FEATURES

However different the causes of occupational tumours may be from the unknown cause of "spontaneous" tumours, the clinical and pathological

features are more or less identical. This is the more evident in that the occupational tumour may appear many years after all demonstrable vestige of the carcinogenic hazard has long since disappeared. There can be no doubt that before the importance of occupational exposures was fully appreciated, tumours were seen in hospital which were in all respects identical and yet belonged in some cases (unknown to the surgeon or pathologist) to the occupational and in others to the non-occupational groups. This fundamental fact must be appreciated in order to realize fully the non-specific character of carcinogens. The manner in which the affected tissue reacts to the carcinogenic insult is non-discriminating so far as the latter is concerned. Thus, a bronchial carcinoma is the same whether it arises from the action of the mysterious "spontaneous" agent or from exposure to chromates; a carcinoma or papilloma of the bladder arising from exposure to certain aromatic amines is indistinguishable from the bladder tumours arising in everyday life; cancer of the lung is indistinguishable whether it arises from radium emanation or from the unknown spontaneous agents. Hence it will be apparent that no better prognosis can be given for occupational than for non-occupational tumours. An advantage lies with the occupational case inasmuch as, the hazard being known, appropriate protective measures can be taken and earlier diagnosis may be possible.

Although the tissue that reacts to potent carcinogenic agents does not discriminate between one or other of them, so far as the qualitative nature of the reaction is concerned, there must exist some difference as between individual tissues and between individual members of a species in the "mechanisms" of response to, or detoxication of, carcinogens. The same principle applies in occupational carcinogenesis. Thus, absorption of any of several aromatic amines over a period of years leads to tumours of only one organ, the bladder; great variation between individual members of a working team occurs, inasmuch as some develop tumours in a few years, others after many years, some after having left the industry altogether, and still others not at all.

Such individual variation is a commonplace in experimental work with animals bred with every precaution to approach genetic uniformity and used only at the same age, of the same sex, fed with the same diet, of the same weight, and so on. In spite of these precautions against variability of response to any given agent, toxic, carcinogenic, pharmacological, and the like, responses are obtained which require statistical treatment in the same way as a population of individuals. In other words, if a single individual is taken at random from the group of animals to be used for an experiment, it is not possible, however carefully uniformity has apparently been assured, to foretell with certainty what the response of the individual will be; we can only express the response as a probability. What lies at the root of this peculiar but universal individual variation nobody can say, but it clearly lends colour to the life of even a humble mouse or rat. In the case of man any other arrangement is unthinkable. If all men reacted in the same way,

whether psychologically or physically, to external forces, it would require only one severe epidemic to wipe out the species. It may be permitted to quote, in this connexion, a great French mathematical-physicist, Poincaré, who said: "C'est l'asymmetrie qui crée le phénomène", and to translate it freely thus: "Uniformity is death; to have life there must be variation".

A notable respect in which occupational and "spontaneous" tumours differ is that whereas in the latter it is as yet impossible to foretell when or where a tumour is likely to arise, in the former the clinical eye can be guided to the region in which tumours are likely to occur. Human mammary cancer has been shown sufficiently often to have familiar characters to render rational a look-out for its occurrence in sisters and close female relatives in the appropriate family. But it is rarely that a medical attendant inquires into the family history of a member of his panel *before* disease begins.

On the other hand, the medical observer in an industry involving a carcinogenic hazard knows or suspects where tumours will occur and directs his scrutiny to those parts. Thus, whereas in the manufacture of briquettes (patent fuel) attention will be directed to the incidence of skin tumours on the head and neck due to pitch; in the cotton industry with a hazard due to mineral oil the part to observe is the scrotum.

Accepting the general principle that the anticipation of the development of an occupational tumour permits of much earlier diagnosis, it is manifest that for any real value to attach to it, it must be possible to say that the disease thus diagnosed can be cured or the condition improved.

SELECTION OF WORKERS

Before proceeding to consider some aspects of occupational carcinogenesis more closely, a word must be said about the selection of workers for industries entailing a cancer hazard. Nothing is easier than to compose a pontifical statement on the medical requirements to be fulfilled before a worker is engaged to work in an industry in which sooner or later there is a danger of his developing a tumour in some region or other. But too much dogmatism in laying down criteria of employability is ill-advised.

The genetic factor.—A common demand is that there should be no history of cancer in the prospective employee's family. Indeed, in respect of one type of occupational tumour, I have made such a statement. But to what extent is there evidence that the liability to cancer in certain kinds of industry is increased by a family history of the disease? The answer must depend to a great extent upon one's own experience and presuppositions. Thus, I have observed the same occupational cancer develop in a father and a son, in two brothers, and in two or three members of the same line, all employed at different times in the same factory. This is a very different thing from saying that there is a family tendency unless a great deal more evidence is obtained, for each of these observations may have been due to chance. But it is undesirable to run the risk of a family build-up unless the

improvement of conditions of work is so great as to have reduced the hazard to vanishing point.

The age factor.—Another criterion often insisted upon is that the prospective employee should be a young, healthy adult. A formula of this kind is liable to be given as almost self-evident. Assuming that a considerable carcinogenic hazard still exists in a factory, the presumption in the formula is that a young, healthy man is less likely to develop an occupational tumour than a middle-aged or not completely fit person. We know of no evidence for such a presumption.

The determinants of the development of occupational tumours are *length and intensity of exposure* to the carcinogenic agent, and the individual power to detoxicate or inactivate the carcinogen. Consider the experience in this country in the case of pitch and tar epithelioma and in shale and mineral oil epithelioma of the skin. Of the former actual cases some 60 per cent. occur after 20 or less years of exposure, whereas of the latter only some 3 per cent. occur after 20 years or less of exposure, and some 64 per cent. occur after 55 years or less of exposure. Thus if a young man, of say twenty years of age, enters operations involving contact with pitch and tar or tar products and if he develops a tumour, he has a 60 per cent. chance of doing so before he is forty. If, on the other hand, he undertakes work involving contact with shale or mineral oil, and if he develops a tumour, the corresponding chance is only 3 per cent. Thus, it does not seem unreasonable to say that it is less fair to put a young man on to pitch and tar work than on to shale and mineral oil work. This does not mean that we regard middle-aged men as something to be sacrificed. Far from it. It means that a middle-aged man may run most of his life's course before he gets a tumour at all. Latency of the occupational tumour in ordinary industrial conditions should always be fully understood before any statement is made on the desirable age for new starters in the hazardous operations.

The health factor.—It will be clear that "health" in a prospective employee must be interpreted in the light of the hazard into which he is about to enter. In the first place, if the carcinogenic hazard is one affecting the skin, it is apparent that skin diseases (e.g. warts) or sensitivities should preclude from entry; if the hazard is one involving a carcinogenic dust, it is clear that any condition which induces any measure of dyspnœa must be precluded, e.g. asthma, bronchitis, obesity, cardiac conditions, even when these are not sufficiently troublesome to prejudice ordinary working capacity; if the hazard involves a carcinogenic effect on the urinary tract, it is obvious that any degree of urinary dysfunction or infection must be precluded; if we may include cleanliness as an adjunct of health, then a dirty worker should never be permitted to continue working in a dangerous toxic process; finally, since the health of a man may have much to do with his habits, it is essential to prohibit nail-biters, tobacco-chewers, snuff-takers, surreptitious suckers of sweets and partakers of snacks.

Intelligence in the worker.—It is best to employ intelligent workers on

processes which involve the subtle and furtive hazard of an industrial carcinogen. The overt manifestations of acutely toxic effects will more or less readily impress themselves on the mind of the least endowed workman, especially if there is danger of what is called "gassing" or if there is evidence of irritant fume or dust. When dealing with liquids or non-irritant dusts or solids, it is much more difficult to impress the average workman. Now, a carcinogenic hazard must involve an employer in the moral obligation to inform his workers minutely on what is involved. The reaction of a worker to such information depends upon his intelligence, for, provided the employer goes to the limit in precaution and the informed workman exerts all his faculties in careful operation and good housekeeping, there is good and reasonable ground for confidence in his safety. But it will not be overlooked that we have used the phrase, "provided the employer goes to the limit". Mere adherence to statutory requirements in the Factories Act, Regulations and Orders is not enough; these are minimum, not optimum.

CARCINOGENIC AGENTS

I proceed now to consider occupational carcinogenesis more especially in relation to the industries or occupations in which it is observed.

If we ask the question, what are the occupational carcinogens, the answer must satisfy criteria that the substances indicated are carcinogens experimentally and that they produce cancer in man in industry. To demonstrate unequivocally that a substance is a carcinogen we must have recourse to animal experiment. Thus, although the relation between coal tar and occupational skin tumours was discovered as long ago as 1875, there was a hiatus of forty years before Japanese investigators produced definite malignant epitheliomas by applying coal tar to the ears of rabbits. Since those days a host of compounds has been tested on animals, and unless a material suspected of producing occupational tumours yields positive results in animals of one species or another we cannot say more than that it is suspect. This is the position at the present time with chromates; evidence in favour of their producing occupational cancer of the lung is strong, but they have never been shown to do so experimentally.

It must be emphasized, however, that we are far from being able to say that because a particular substance is a carcinogen to animals it is also a carcinogen to man, and it would be dangerous to conclude that because it has not been shown to be a carcinogen in animals that it is therefore not a carcinogen to man. The demonstration of carcinogenic properties in animals engenders a reasonable fear that the material involved may also be carcinogenic to man. But the demonstration of carcinogenicity in man may never be possible. Thus, the notorious dye "butter yellow", *p*-dimethylaminoazobenzene, is indubitably a liver carcinogen to a variety of species and has long been forbidden as a food colour, but no evidence that it has ever had carcinogenic effects in man has been, or ever will be, obtained. Many azo compounds have been shown to possess carcinogenic properties in animals, but

no reasonable evidence has ever been obtained that men in a dye factory handling only uncontaminated azo compounds, including azo dyestuffs, are especially liable to develop tumours. On the other hand, it has never been shown that the dye intermediate, benzidine, is a carcinogen to animals, but there is no reasonable doubt that it is a carcinogen to man.

It has recently been pointed out by Salter (1948) that "despite a wealth of data indicating carcinogenesis in man from crude mixtures, only three *unadulterated* agents have thus far been *proved* carcinogenic for man. These are (a) radiation, (b) beta-naphthylamine and (c) arsenic".

RADIATION

The evidence for skin carcinoma in white workers much exposed to sunlight in tropical or semi-tropical lands is widely accepted. The effect of intense ultra-violet light on the much thinner skin of rodents is to produce sarcoma or mixed tumours, the difference probably being that whereas the relatively thick horny layer of man absorbs the ultra-violet radiation, in the rodent the latter penetrates to the subepithelial layers and acts on the connective tissue there located.

X-rays.—Statistics of the incidence of cancer and related conditions (e.g. leukæmia) among radiologists, X-ray tube makers and technicians show a definite occupational hazard for these workers. The direct demonstration of the development of tumours of the skin from exposure to X-rays has been made during the treatment of certain skin conditions with this agent, e.g. hypertrichosis of the face, psoriasis, lupus. The final confirmation of the carcinogenic action of X-rays was made by exposing the skin of rodents for many months to this action; spindle-cell sarcomas developed.

Radioactive substances.—As long ago as 1879, it was shown that the rapidly wasting disease with manifest pulmonary damage which had for centuries been observed in miners in the Erz Mountains (between Saxony and Bohemia), was due to a circumscribed lung tumour. In subsequent years there were various theories of the ultimate cause of the condition (e.g. uranium, cobalt, arsenic), but the measurement of the radioactivity in these mines in the early 1920's left no doubt that the miners were inhaling very large amounts of radioactive material, whether as actual radium compounds or as radon gas. An interesting feature of these tumours was, and still is, that the lung tumours may not appear until many years after the miners have left the mines altogether. This latency is so frequent an accompaniment of occupational tumours as to be almost a specific character of them.

The alarming recognition years ago, both in this country and in the United States, that persons engaged in the application of radioactive compounds to surfaces and in the introduction of such compounds into glass tubing (luminizing operations) were liable to develop severe anæmia of aplastic type and sarcoma of bone, led to the important Luminizing Order of 1942. This order is meticulously designed to prevent the ingestion and

inhalation of radioactive material during work, and the contamination of skin, hair and clothing and items in the environment with it.

The final confirmation experimentally of the carcinogenic effects of radioactive materials has been produced in the years since the end of the 1939-45 war, as a result of work with plutonium (Pu_{239}) and fission products of uranium (U_{235}). Thus, 1μg. of Pu_{239} injected into mice will produce sarcoma at the site of injection; deep penetrating radiations (γ) lead to blood disease, and the less penetrating (α) to cancer of the skin in all animals exposed.

Thus the proof of the carcinogenicity of these various kinds of radiation is complete. It is fortunate (or unfortunate, according to the point of view) that the detection of dangerous conditions of work or dangerous levels of absorption is carried out by highly precise physical methods (e.g. calibrated photographic films, Geiger-Müller counters), and hence it should be possible to eliminate serious hazard. Observation of the manner in which safety measures are installed and operated in handling compounds of radium and radioactive isotopes leaves little doubt that, except in the case of accident, the safe tolerated dose of radiation (0.3r-0.5r per 5-day week) will not be exceeded.

AROMATIC AMINO COMPOUNDS

Salter's inclusion of β-*naphthylamine* as a fully demonstrated carcinogen rests upon increasing knowledge of the remarkable incidence of bladder tumours among workers engaged in the manufacture of dye intermediates, i.e. aromatic amino compounds from which, with other compounds of greater or less complexity, the final dyestuff product is built up. Whereas the original description of a suspiciously high incidence of bladder tumours in this industry goes back more than fifty years, the impress of the disease upon countries in which a big-scale dyestuffs industry was developed relatively late became manifest only in the last twenty years or so (e.g. U.S.A., Britain and even more recently France).

Several aromatic amines were for a good many years suspected as the carcinogens responsible, e.g. aniline, benzidine, α-naphthylamine and β-naphthylamine. Only in the last ten or twelve years has experimental evidence been obtained in dogs that one of these compounds, β-naphthylamine, is indeed a potent carcinogen.

Although several workers, two in America and one in Britain, have obtained tumours in dogs or bitches with large doses of this compound administered for several years, the report of Gehrmann, Foulger and Fleming (1949) has shown that 300 mg. of β-naphthylamine, administered daily for five days a week until fifty doses had been given and produced in dogs (several groups of three or four) many signs (urinary and cystoscopic) premonitory of the development of tumours. The minimum time for this effect was fifty days. Cessation of administration of the compound was followed by return of the bladder to what seemed a normal condition in a few weeks. But carcinoma was found in one bladder at autopsy six-and-a-half years later, and pre-neoplastic changes in another. This latter observation is the counterpart of what happens to workers who after some years of exposure in the industry may leave it apparently unscathed, and develop a bladder tumour many years later. For a sub-

stance to produce this effect after only fifty days of administration qualifies it to be included among the most potent carcinogens.

Gehrmann *et al.* (1949) made the further observation, by exactly similar experiments on bitches, that benzidine (171 mg. daily for 5 years), pure α-naphthylamine (301 mg. daily for 4½ years) (α-naphthylamine as manufactured in this country contains 3-5 per cent. β-naphthylamine and has been known for many years to produce tumours in the bladder); aniline (300 mg. daily for 2 years), tolidine, 230 mg. daily for 3 years, and dianisidine, 291 mg. daily for 3½ years, produced no tumours in any of the twenty-four dogs used for these compounds.

Similar experiments in this country have also failed to show that aniline and benzidine are carcinogens in animals.

Occupational *cancer of the bladder* is a notifiable and scheduled industrial disease in most countries where the problem arises (e.g. U.S.A., Germany, Switzerland, France, Italy), but not in Britain. The disease is especially interesting for its almost exclusive attack on the bladder; very rarely a primary tumour of the renal pelvis or ureter is seen. It may start as a non-malignant papilloma or as a carcinoma, very often in the trigone and perhaps most frequently in the vicinity of the ureteric orifices. The dilemma is obvious if the condition is to be described as an industrial disease in the manner employed in this country; that is, with specification of the process, not merely the industry.

ARSENIC COMPOUNDS

Cancer of the skin among workers exposed to the hazard of absorption of arsenic compounds has been known for more than a hundred years. Ullman, in his well-known "Handbook of Skin and Venereal Diseases", gives a collection of 72 cases of cancer attributed to arsenic, most of which were due to long treatment with arsenical preparations. Sir Thomas Legge in this country, nearly fifty years ago, associated the familiar skin changes induced by arsenic compounds, pigmentation and hyperkeratosis, with irritation of the upper air passages and perforation of the nasal septum when the hazard was an arsenical dust.

Cases of *skin cancer* have been described among a great variety of workmen in contact with arsenical compounds, for example, men in arsenic mines, in tin foundries, in preparing or using arsenical sheep-dip, in copper smelting, in glass-factories, and in the handling and use of arsenical pesticides.

Intermittent reports appear of *lung cancer* in workers handling arsenical compounds. Thus, in his 1943 Annual Report, the Senior Medical Inspector of Factories stated that "The etiological relationship between malignant disease of the lungs and exposure to arsenical dusts is a matter of importance . . . The number of cases which has come to our notice is, however, few . . ." Between 1939 and 1943 four such cases were notified, all in workers with sheep-dip containing sodium arsenite. Currie, a Medical Inspector of Factories, in a recent article (1947), refers to a fatal case of a columnar-celled adenocarcinoma of the lung in a worker who had been exposed to arsenical

dust for forty-three years, and to one of skin cancer complicated by lung cancer in a worker in arsenical insecticides.

The clinical evidence in favour of the carcinogenic action of arsenic is undeniably strong, but the experimental evidence with animals is surprisingly slight.

Leitch and Kennaway's frequently quoted experiments were on painting mouse-skin 3 times daily with a 1.8 per cent. alcoholic solution of potassium arsenite. This highly toxic solution had to be replaced by a 0.12 per cent. solution. After 86 days, the experiment yielded one animal out of 100 with a squamous-celled epithelioma and Leitch's own later experiments yielded no tumours at all. There were many fatalities. Hyperkeratosis and hyperpigmentation produced by arsenic have been demonstrated by other investigators.

Reviewing the evidence, it seems reasonable to agree with Salter (1948) that radiation, β-naphthylamine and arsenic can be identified as carcinogenic agents in man, and that there is varying weight of evidence that they are also carcinogenic in animals.

OTHER OCCUPATIONAL CARCINOGENS

We must now consider whether or not in other cases of known or alleged occupational carcinogens an identifiable cause can be held to be responsible.

When in 1915, Yamagawa and Ichikawa produced skin carcinoma on the external ear of rabbits by repeated applications of *coal tar*, and Passey in 1922 induced malignant growth on the skin of mice with ether extracts of soot, the stage seemed to be set to identify the active compounds in these complex mixtures. From this period began the remarkable work of Kennaway and his school: the demonstration by Kennaway of the carcinogenic properties of tars obtained by pyrolysis from mineral oil, coal, skin, yeast, hair, and by subjecting relatively simple saturated and unsaturated hydrocarbons to heat in the presence of hydrogen; the study of the characteristic fluorescence spectra of carcinogenic tars and oils and the later recognition that the polycyclic hydrocarbon 1:2-benzanthracene possessed a fluorescence spectrum of a similar character; the syntheses of homologues of benzanthracene leading later to a great increase of synthetic carcinogens; the isolation from coal tar pitch of a pure hydrocarbon which showed the characteristic spectrum and was a potent carcinogen, and its later identification as 3:4-benzpyrene; and the relatively recent recovery of about 75 mg. of pure benzpyrene from 10 g. of crude tar distillate. It may safely be supposed that the actual benzpyrene content of tar is very much more than this having regard to inevitable losses in purification.

The chain of evidence seems complete that 3:4-benzpyrene is the constituent in tar responsible for human cancer *but there is no direct evidence that this is so.* No doubt evidence will appear that the omnipresent town-soot contains similar or identical carcinogenic hydrocarbons, but its reference to the incidence of, say, cancer of the lung (which is certainly on the increase) will be hypothetical until the relation between animal carcinogens and human carcinogens is established.

Asbestos.—As long ago as 1938 the suspicion arose that asbestos workers might be more than normally prone to lung cancer.

Nordmann (1938) analysed six cases of lung cancer and showed that the range of exposure periods was 7 to 21 years, and the range of intervals between entering the industry and death was 15 to 21 years. The malignant disease in some cases occurred years after leaving the industry. Half of these cases were comparatively young, 35 to 41 years of age at death. In one remarkable case a seventy-one year old woman had worked in asbestos for only 19 months. Later in the same year he referred (1938) to a further seven cases of associated asbestosis and lung cancer, including Gloyne's finding of six cases of carcinoma of the lung in 50 autopsied cases of asbestosis.

In the 1947 Annual Report of the Chief Inspector of Factories, the Senior Medical Inspector tabulated the age incidence among 235 deaths caused by asbestosis: in 13.2 per cent. of these cancer of the lung was present, and it is especially important to note that 4.8 per cent. of the age-group twenty-five to thirty-four, and 5.6 per cent. of the age-group thirty-five to forty-four had this condition. It will be seen that the over-all figure is closely in agreement with Gloyne's findings.

The establishment of the well-known diffuse pulmonary fibrosis induced by exposure to asbestos fibres is usually regarded as due to mechanical action, and some evidence of this is presented by finely grinding the asbestos to particles less than 2μ in length, whereby the fibrosis effect is eliminated in animal experiment. The reverse would be the case with silica. But when so much has been said, it still remains a puzzle why cancer should favour the asbestosis lung and not the silicotic lung. Silica is held to act by local solution and chemical action: asbestos (a hydrated magnesium silicate) is held to act as an irritant in virtue of its physical form. The next step, to bring cancer in the asbestosis lung into line with a chemical theory of cancer, has not been taken.

Nickel carbonyl.—It has been known for a long time that workers in nickel refineries develop remarkable tumours of the ethmoid region of the nose and bronchogenic carcinoma of the lung. Like so many other occupational cancers it may occur many years after exposure to the carcinogen has ceased.

Amor's (1939) interesting analysis of ten cases of cancer of the ethmoids and four of lung cancer shows that the average period from first exposure to the hazard (*vide infra*) until death was some 17 years (range 11-28) for cancer of the ethmoids and 20 years (range 9-27) for cancer of the lung. In this series the nasal tumours attacked the middle turbinates and the ethmoidal air cells. These were all carcinomas of various kinds, squamous, columnar-celled and undifferentiated.

I introduce nickel into this short discussion mainly because its association with the problems of occupational cancer is a very good example of a cryptic cause.

In the separation of nickel from its ores the problem before the technologist is to fractionate the ore in such a way that not only nickel but several other valuable metals always found in association with nickel will also be recovered. It is the manner in which this fractionation is carried out which determines whether or not the process will include the hazard of cancer. Nickel is usually extracted in this country from Canadian ore and the latter must undergo a considerable number of processes before

it is rendered suitable in nickel content for the process of electrolysis or the Mond procedure (formation of nickel carbonyl and its subsequent decomposition by heat). The original ore consists of a number of metallic sulphides (Cu, Fe and small amounts of Co and rare metals) deposited in rock. By processes of flotation the rock can be deposited from the ore and various levels separated off which permit a top layer rich in copper and nickel. By calcination of this, SO_2 is liberated and converted to sulphuric acid and acid sodium sulphate. Further treatment in a reverberatory furnace and then in a Bessemer converter permits of a final product ready for refining which may contain up to 80 per cent. (Ni + Cu).

The modern first process of refining is to heat this product with $NaHSO_4$ and coke, which yields a molten product consisting of two layers, an upper solution of CuS in Na_2S and a lower of nickel sulphide. This process is repeated to produce a better product. But the copper can also be removed by treatment with sulphuric acid and recovery as copper sulphate, and this was the method used in the British factories. In either case the residues after removing copper in one form or another consist mainly of metallic sulphides and must undergo drying, grinding and calcination to produce metallic oxides, all very dusty operations. A long time had clearly to elapse before the danger could be realized. Having regard to the nature of the disease it could hardly fail to be realized that a dust hazard was involved.

In the subsequent processes of refinement, whether by electrolysis as used in Canada or the carbonyl process as used in Britain, the hazard is of a quite different kind. The latter process, which was regarded with suspicion by some, involves the reduction of the oxide by means of water gas (60 per cent. hydrogen and 36 per cent. carbon monoxide) kept at about 350° C. by hot air circulation. Now although both hydrogen and carbon monoxide are reducing agents, at the low temperature at which the reaction is run nearly all the reduction is due to hydrogen. The effect of this is to use up the hydrogen and enrich the emergent gases in carbon monoxide. The crude metal is now made to meet the CO-rich water gas; the nickel combines with the CO and forms a very volatile compound $Ni(CO)_4$—nickel carbonyl—which is carried over as gas to be decomposed at 180° C. on heated nickel pellets, on which the liberated nickel is deposited; the liberated CO being re-used to form more carbonyl. The further processes of extraction of rare metals and cobalt need not concern us here.

The point was to discover the carcinogen in this complicated process once it had been made clear that both ethmoid and lung cancer were prevalent. Let it be said at once that neither nickel nor nickel oxide nor nickel salts could be shown to be carcinogenic in various experiments. Further (as stated by Amor) the incidence of malignant disease among workers in exactly similar conditions of process and work in Canada was not increased, *but the Canadian process did not include the use of sulphuric acid for the separation of copper*. Nickel carbonyl itself is a highly toxic product and when inhaled it is decomposed with the deposition of nickel in the lung and liberation of CO. This evidently constituted the rationale of the testing of finely divided metallic nickel for carcinogenic properties.

Nickel carbonyl poisoning in man leads to pulmonary œdema and cerebral and pulmonary hæmorrhages; in animals the same effects can be demonstrated as well as hæmorrhages in the bronchi and trachea and nasopharynx, and sometimes in the adrenals. These facts, combined with the freedom from malignant disease of men engaged in the manufacture of nickel carbonyl, and the additional absence of evidence of ethmoid or lung cancers among men getting the ore or carrying out the pre-refining processes, left the extraction of the copper from the matte to be studied.

The difference between the Canadian and Mond processes was the use of

sulphuric acid for the extraction of copper and in this sulphuric acid a high content of *arsenic* was eventually found. In the period relevant to the present discussion an ordinary commercial sulphuric acid of specific gravity 1.7 might contain 3.18 g. As_2O_3, 2.56 g. As_2O_5 per litre (*Chemical Trade Journal*, 1906), and so would readily form insoluble arsenical compounds of copper (including arsenides). Removal of the copper sulphate would leave the residual nickel and other metals still contaminated with Cu-As compounds. On drying, grinding and calcining, enormous amounts of arsenic-rich dust would be evolved and, as proper precautions were certainly not taken forty or more years ago, the stage was set to produce the slowly developing arsenical cancers. In spite of vast improvements in process and safety, cases still arise in this country among men who had been exposed to the old process and to which their condition must be attributed. The attribution of the tumours to arsenic is, of course, an inference, but one based upon almost incontrovertible evidence.

CONCLUSION

It is not possible in a short article to enter adequately into the many other inducers of occupational tumours, e.g. chromate, beryllium, and the industrial materials which produce blood diseases simulating neoplastic disease, e.g. benzene. Research continues apace in academic and industrial laboratories to cast more light on the nature of more obscure occupational conditions.

As the civilized world becomes more and more dependent upon the products of industry, and the persistence of chemists brings to light more and more complex compounds with desirable or often undesirable properties, it is the business of experimentalists in the physiological, pathological and biochemical fields to elucidate their effects on man and try to protect mankind from its own ingenuity.

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VOCATIONAL PSYCHOLOGY

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One of the outstanding characteristics of our contemporary society is the apparently haphazard nature of the occupational choice in many cases; and not only by young people of limited education and intelligence. Before the war there was current a well-quoted story of a judge who confessed that his choice of the Bar had been determined entirely by the chance remark of an acquaintance after he had made a speech while training for a totally different calling. Such situations are by no means rare and admittedly do not always result in failure, as evidenced by the judge, but it is the experience of many doctors, particularly general practitioners and industrial medical officers, that there are too many occupational misfits who are a source of illness and unhappiness to themselves and their families. Very often it is too late to do much about such cases in middle age; the claims of training, experience, family commitments and pension funds all militate against a change. Some individuals escape into illness and take the maximum amount of sick leave; others just grumble; whilst the more fortunate get their satisfaction out of gardening, carpentry or amateur dramatics. As the years go on, many individuals find a fairly satisfactory adjustment, but the frustration is an important contributory factor in many psychosomatic illnesses.

THE MISFIT IN INDUSTRY

Although these problems are more clear-cut in the more intelligent and higher income groups, the greater incidence falls among the less enlightened members of the community. In the report of a vocational guidance experiment conducted among twelve hundred elementary school children in London before the war, the investigators summed up their conclusions in these words:—

> "When the question 'What do you want to do when you leave school?' was followed up by 'Why do you want to do that?', it was clear that many fortuitous factors were influencing the choice. Not infrequently it seems to be a matter of fashion, and it was not without interest that the current reply seemed to vary from week to week when the same question was put to the same child by different investigators".

The outstanding feature of adolescent attitudes is the immaturity of the normal child of fourteen, and the reasons for occupational choice are often quite irrational. Frequently the attraction seems to be due to some quite superficial aspect, as in the case of the boy who wanted to be a plumber so that he could mend the frozen pipes at home and thus help his mother. Such an attitude is scarcely a satisfactory background for deciding on work that is going to occupy a third of an individual's whole life.

A similar inquiry was carried out by Hawkins in a Midlands Central School. These youngsters were asked to state, not only the occupations

which they would *like* to follow, but also the occupations which they would decline to follow. The investigator has thus summed up his conclusions:—

"We can now see on what factors the pupils of this school as a whole are mainly basing their choices and refusals of work most frequently. These motives are cleanliness, pay, security, health and a liking for the work . . . It is also evident that there are certain reasons which are of primary importance in choosing a really suitable occupation, but which are rarely mentioned at all; these are the suitability of the individual concerned, mentally, physically, or in temperament or character".

Estimates of how many misfits there are in Great Britain have varied from 5 to 50 per cent., which is perhaps evidence of the difficulty of the subject. It is often difficult to draw a line between those people who should be regarded as completely maladjusted and those who do their jobs well enough but would have done better at something else. In this connexion an opinion expressed by the late Sir Duncan Wilson, the former Chief Inspector of Factories, may be quoted:—

"Just as present sufferers of silicosis must inevitably remain incurable victims of past ignorance, so must adult workers remain for the most part unaffected by the progress in industrial psychology. The trend of development is, and should be, in the direction of studying the potential worker—the child—and it is in that field where I prophesy that the most useful present-day application of industrial psychology lies".

VOCATIONAL GUIDANCE

It is difficult to get incontrovertible proof of the value of vocational guidance, but all the available evidence goes to show that boys and girls who have been appropriately advised tend to like their jobs more, to stay in them longer and to get better reports from their employers than those who have not.

It is sometimes thought that vocational guidance depends to a large extent upon *intelligence tests*, but in reality these form only one aspect of a total appraisal. Intelligence tests are not tests of knowledge, for they are designed to measure our ability to use what we know, not to find out how much we know, and have proved to be reliable and useful instruments for diagnosis, especially in the younger age-groups. In adults, a rough grading of types of work involving intelligence in gradually diminishing amounts is as follows:—

(1) Higher professional and administrative workers
(2) Lower professional, technical and executive workers
(3) Clerical and highly skilled workers
(4) Skilled workers
(5) Semi-skilled repetitive workers
(6) Unskilled repetitive workers
(7) Casual labour
(8) Unemployable individuals

When it is said that intelligence tests are reliable, it means that a person tends consistently to get very much the same score, however often he is tested. The most effective type of intelligence test is an individual test, given by a trained psychologist, and this is advisable when the problem is to help

a young person to choose a career. However, if the problem is to make a broad classification of a large number of persons according to whether they have high, medium or low intelligence, a group test is satisfactory and much quicker. *Group tests* have been widely used in the Forces, schools and industry.

A certain minimum of general intelligence is necessary for regular employment, but there are few jobs in which high intelligence is the chief requirement for success. There is a wide range of jobs within the intellectual capacity of the average person, and in these success often depends primarily upon the extent to which the worker possesses the special ability demanded by the particular job. Much research has been done in these fields, and it appears clear that these abilities are innate since neither intelligence nor enthusiasm can overcome their relative absence appreciably. In industrial work, the abilities most commonly needed are manual dexterity and mechanical aptitude. There is considerable evidence to support the popular contrast between the heavy-fisted and the light-fingered. Dexterity depends partly upon the power to control and coordinate a number of different muscular movements, which are naturally affected by emotional stability, fatigue and practice. Many tests of manual dexterity have been devised but their correlation with subsequent attainment is not always statistically significant. One of the most simple examples of this type of test is that used for predicting skill as a jeweller, which consists of bending various lengths of wire to a given design. Mechanical aptitude is assessed in a wide variety of tests and there is evidence to show that there is a common element involved in all mechanical jobs. This common element is what is meant by the term "mechanical aptitude" and can be tested very satisfactorily.

Since the days of Greek civilization, when Galen first classified men into four types, philosophers and doctors have been seeking a satisfactory classification of temperament. Many tests in this field have been devised but are not sufficiently reliable to justify general acceptance. Temperament must still be determined by an interview and there are, of course, great differences in people's interviewing skill. Some doctors have developed an intuitive understanding of other people that helps to put individuals at their ease and express themselves freely. Not all doctors realize the value of listening objectively as opposed to a rapid question and answer technique. Actually there are various types of interview and some are easier to conduct than others. In the interview for selecting or transferring a worker, the psychological problem is to weigh up the candidate and decide whether his total personality is suitable for his new job and also for the occupational setting in which it will be done. Interviews should be held whenever possible in pleasant surroundings. An interviewer is primarily a good listener, but he must also be capable of good talking, so that he can reassure an over-anxious "interviewee". Above all, he must have a genuine, but detached, interest in people and be able to convey this to those with whom he is in contact.

The crucial test of a person's suitability remains his behaviour in action

and if after a suitable period an individual proves unsuitable or is unhappy in his work, a suitable change should be made. An unsuitable supervisor can cause not only much unhappiness but also much psychosomatic illness among departmental employees.

ANALYSIS OF CASE STUDIES OF MISFITS

There are many occupational misfits whose troubles, although serious enough, do not drive them into the hands of the police, nor into the consulting rooms of psychiatrists. Thus, Macrae (1934) has published details of 50 consecutive cases of dissatisfied workers examined at the National Institute of Industrial Psychology. The ages ranged from seventeen to forty-five, and the degree of intelligence ranged from something near genius to something near mental deficiency. Their academic attainments ranged from those of the highly distinguished graduate to those of the backward elementary school pupil. Their occupations included factory work, retail selling, commercial travelling, the Army, agriculture, engineering, banking, office work, industrial management, journalism, law, teaching and the higher Civil Services.

In many cases the causes of failure were multiple, but of the 50, 16 had work unsuited to their intelligence—of these 16, 10 had too much intelligence for their jobs. This group included 6 very able young men who had taken up routine clerical work in situations where promotion was extremely slow. Two other members of the group had such severe personality disorders that it appeared unlikely that they could ever occupy positions compatible with their first-class intelligence. In addition, there was the case of a bright elementary schoolboy whose repeated illnesses had prevented his attending for a secondary school scholarship, with the result that his lack of technical training prevented his getting work commensurate with his abilities. Here again, one sees the close connexion between physical health, occupational adjustment and subsequent happiness in life.

Equally sad is the plight of the individual whose work demands higher intelligence than he actually possesses. Many doctors have come across the "dull-normal" public schoolboy who has managed to get through school certificate after a number of failures and is then apprenticed to a profession making higher demands on his ability than he can face up to.

PHYSICAL CHARACTERISTICS AND VOCATIONAL PSYCHOLOGY

Martin Leaker and Smith (1942), who have had considerable experience in selecting and training workers in the North of England, have recommended that firms which do not have their own full-time medical staff should make part-time arrangements with a local general practitioner with industrial experience to carry out medical testing for them. They pointed out that the use of medical tests does not have the effect of excluding all but thoroughly healthy individuals, but that it allows more than the "grade I" candidates to be engaged. They justify this opinion by saying that an interviewer

without medical experience is inclined to run no risks and to reject healthy applicants simply because they have a poor complexion or a physical deformity.

The Vocational Guidance Department of the National Institute of Industrial Psychology has drawn up the following list and suggests that medical practitioners should underline, for the information of personnel managers, the occupational conditions or requirements which would *not* suit the individual in question:—

Muscular strain	Righthandedness
Constant walking	Hot working conditions
Constant standing	Cold working conditions
Constant sitting	Damp working conditions
Constant stooping	Exposed working conditions
Acute hearing	Dusty working conditions
Acute vision	Indoor work
Colour discrimination	Nervous strain
Dry hands	Climbing
Handling foods	Risk of falls.

The industrial medical officer has always played an important part in industrial placement, and the development of associated scientific methods has enhanced the importance of the medical contribution. To an increasing extent emphasis is placed to-day on the individual's physical and mental capacities rather than on his defects.

THE PLACEMENT OF HANDICAPPED INDIVIDUALS

The current emphasis on full employment and the desire of all concerned to employ disabled people whenever practicable has thrown added responsibilities on to the industrial medical officers.

The definition of disablement is not easy. We are none of us physically perfect, and abnormality is a matter of degree. It is, nevertheless, quite apparent that a large number of people need help and skilled occupational placement on account of deformity, disease or injury.

How many people in Great Britain need various kinds of help? Even a rough guess is difficult. There has been no comprehensive survey of disablement in the United Kingdom, but a large survey made in the United States in 1935-36 showed that about one-sixth of the total working population needed special help in finding or holding employment because of some disability, but less than a thirtieth needed more than careful placement in a suitable job. A more recent survey in Sweden roughly confirms American estimates of the scale of the problem.

The basis of resettlement work in Great Britain was laid by the Tomlinson Committee, which set forth certain basic principles that should govern policy for the rehabilitation of the disabled. These objectives have been implemented in the Disabled Persons (Employment) Act, 1944. To make it quite clear who was entitled to special help in getting employment, the Act provides for the maintenance of a Disabled Persons' Register on which persons entitled to this help can be enrolled if they so wish.

MEDICAL REHABILITATION

The reduction of the incidence and severity of disablement is primarily a medical problem and depends upon the organization and efficiency of preventive and curative medicine. In progressive hospitals the records of all hospital patients likely to have a residual disability are discussed at a weekly meeting of the rehabilitation medical officer, the almoner and the disablement resettlement officer of the Ministry of Labour. The need for vocational training and post-hospital reconditioning at a rehabilitation centre is reviewed, and advice is given on placement in the most suitable jobs.

Post-hospital rehabilitation, in so far as it is a continuation of medical rehabilitation, merges into industrial resettlement, and the final stages of recovery from injury, disease or psychiatric illness are inseparable from the social and economic problems of readaptation to life and work. Persons needing industrial rehabilitation fall into two main classes. Hospital cases no longer in need of more than occasional medical supervision may still have poor physiological response to activity or may not have fully completed their functional recovery.

Post-hospital rehabilitation is still in its experimental stages and the facilities are no longer adequate to the demand. One of the most valuable developments is the opening of thirteen industrial Rehabilitation Units in various parts of the country. Each Centre, which is non-residential and with accommodation for 100 individuals, is under an experienced rehabilitation officer, a part-time medical officer, an industrial psychologist, a trained social worker, occupational supervisors qualified to test suitability in a wide range of occupations, a physical training instructor and a disablement resettlement officer.

The course, which may last from one to three months, is aimed at assessing the individual's employment problem: a preliminary assessment, taking account of functional limitations, vocational aptitudes and the ability to stand up to the exertions of a full day's work. For those likely to be able to return to their previous occupation, the emphasis is on exercises and occupational therapy to restore ability for a particular calling. For those who may have to take up a new occupation, there is also continuing assessment of vocational aptitudes.

It can thus be seen that the problems of vocational guidance for the young, and suitable placement, have many counterparts in the resettlement of those with physical and mental disabilities. The whole emphasis is upon an individual's abilities and skills rather than upon his defects, and this is the outstanding feature of work which is a new and rapidly developing partner of medicine.

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INDUSTRIAL LAW FOR THE GENERAL PRACTITIONER

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For nearly one hundred and fifty years the State has been concerned with the protection of the industrial worker from the hazards of employment. The first protective Statute, the "Health and Morals of Apprentices' Act", dates from 1802, and since then over fifty Acts relating to factory work alone, apart from those concerned with other forms of employment, have been passed by Parliament. The earlier restrictions related to hours of work, night work, cleanliness of workshops, exclusion of young children, education, and the special protection of young persons and women. Later, came prescribed standards for safety, and special restrictions relating to employment in dangerous trades and processes. Since 1833, a Factory Inspectorate has watched over the implementation of the Factory Acts, and since 1850, a Mines Inspectorate has performed the same service for mines and collieries. In 1844, Certifying Surgeons were appointed to certify that children entering factories were at least nine years old, and in 1898 the Inspectorate of Factories was enriched by the appointment of a medical inspector, the late Sir Thomas Legge.

Compensation for disability arising from an accident at work was first granted in 1897, and nine years later the law was extended to include certain occupational diseases. This compensation was granted to all those who came within the definition of "workman" as defined in the "Employers and Workmen" Act of 1875, which stated:—

> "The expression 'workman' does not include a domestic or menial servant, but save as aforesaid means any person who, being a labourer, servant in husbandry, journeyman, artificer, handcraftsman, or otherwise engaged in manual labour, whether under the age of twenty-one or above that age, has entered into or works under a contract with employer, whether the contract be made before or after the passing of this Act, be express or implied, oral or in writing, and be a contract of service or a contract personally to execute any work or labour".

Under more recent legislation, occupational lung diseases, notably silicosis and asbestosis have been made compensable, and the Act of 1946, by including "loss of faculty" as well as "loss of earning power", enlarged the whole concept on which compensation is based.

During the present century successive Governments have been concerned with the growing numbers of persons disabled as the result of war or accident. Since the 1914-18 conflict, many voluntary bodies have been set up and many schemes put forward to deal with this problem. Finally, in 1942 the Government, no doubt alarmed by the mounting civilian casualties of the war, appointed an Interdepartmental Committee under the Chairmanship of Mr. George Tomlinson, M.P., to inquire into the

whole question of rehabilitation and resettlement. The Report of this Committee formed the basis of the Act of 1944.

The general practitioner will not only be expected to give advice to those of his patients who come within the scope of the various Acts but may find himself involved in procedures under these Acts. The purpose of this article is to indicate the various duties which he may be required to undertake under: (1) the Factories Acts; (2) the National Insurance (Industrial Injuries) Act; and (3) the Disabled Persons (Employment) Act.

THE FACTORIES ACTS, 1937 AND 1948

The 1937 Act requires the notification of certain industrial diseases occurring in factory workers to the Chief Inspector of Factories. This must be done by the doctor attending the patient and he must also include the name of the factory in which the patient last worked. Failure to notify constitutes an offence, and the doctor is liable to a fine.

These "notifiable diseases" are fourteen in number and notification of their occurrence is restricted to workers in factories or premises covered by the Factories Act. They are: poisoning from lead, arsenic, mercury, phosphorus, manganese, carbon bisulphide, aniline and benzene (chronic poisoning only); anthrax, compressed air illness (caisson disease), epitheliomatous ulceration from pitch, tar, paraffin or oil; chrome ulceration; and finally, toxic jaundice and toxic anæmia. It should be noted that, although some are the same, the notifiable diseases occurring among factory workers are distinct from the "scheduled" or "prescribed" diseases of the Workmen's Compensation Acts. Lead poisoning occurring in any worker covered by the Lead Paint Regulations of 1927 must also be notified.

Appointed Factory Doctor.—The certifying surgeon of 1844, while still retaining his original title and duties under the Compensation Acts, changed his name in the 1937 Factories Act and became the "examining surgeon". He has now suffered a further change under the 1948 Amending Act and will in future be known as the "appointed factory doctor", a cumbersome title which has called forth some criticism from the profession. These appointments are held almost exclusively by general practitioners and are made by the Chief Inspector of Factories. At present there are about 1800 or so in Great Britain.

The appointed factory doctor is responsible for his official duties to the Chief Inspector, who may revoke or modify the terms of the appointment at his discretion. He is subject to certain restrictions by reason of his appointment, the chief ones being that he may not acquire a financial or other interest in any works in which he has medical responsibilities under the Act, nor may he accept an appointment as a full-time works medical officer or a retaining fee as adviser to employers or workmen. He may not, in his official capacity, visit any works outside his district without special instructions from the Chief Inspector. The appointment is personal, and it cannot be automatically filled by a locum tenens in the absence of the holder;

therefore except in emergencies, previous application must be made to the district Superintending Inspector for the temporary appointment of another practitioner.

The duties of the appointed factory doctor may be summarized as follows:—

(1) To examine young persons under eighteen who are entering employment in factories and other places covered by the Factories Acts.
(2) To undertake the periodic medical examination of persons working in prescribed dangerous processes and of male young persons employed on night shifts.
(3) To investigate and report upon cases of notifiable industrial disease and certain accidents, and to undertake any special investigations at the request of the Minister.
(4) To give evidence in Court when required to do so by H.M. Inspectors of Factories.
(5) To present an annual report and statement of accounts to the Minister.

Medical examinations are usually conducted on the factory premises but the doctor may, with the approval of the Chief Inspector, make other arrangements for the initial examination of juveniles where only a few are employed in any works. Examinations of workers in prescribed processes must be done at the works.

An employer, who has established a medical service in his factory, may apply to the Chief Inspector for his medical officer to be specially recognized for the examination of young persons and those working in prescribed processes. The doctor so appointed then assumes the responsibilities of the appointed factory doctor in these respects for the factory in which he is employed. He has no official duties outside his own factory.

These Acts are administered by the Ministry of Labour and National Service.

NATIONAL INSURANCE (INDUSTRIAL INJURIES) ACT, 1946

This Act is part of the comprehensive social insurance scheme recently established. It introduces a new principle, in that workmen's compensation is no longer regarded as the employer's liability but becomes a responsibility of the State. Monetary payments are now made not only for loss of earning power but for "loss of faculty", for example, disfigurement or the loss of an eye or a limb which might not in itself interfere with the individual's ability to earn his living. Three types of benefit are made under the Act:—

(1) Injury benefit, which is a weekly payment for disability for a maximum of twenty-six weeks from the date of the accident or onset of disease.

(2) Disablement benefit, for those whose disability continues longer than twenty-six weeks, or is permanent.

(3) Death benefit payable to dependants.

A *permanent disability* which is assessed at less than 20 per cent. is compensated by a small lump sum payment instead of a pension, otherwise no provision is made for this type of payment and pensions cannot be converted into lump sum settlements. All types of benefit carry additional allowances for certain dependants. Payment in all cases is made from a central fund to

which workers, employers and the State contribute. Claims are lodged in the first instance with the insurance officer at the local office of the Ministry of National Insurance and should be accompanied, although this is not obligatory, by a certificate from the claimant's own doctor. The initial assessment of claims rests with the insurance officer, and this responsibility is eased if the doctor certifying disability can express an opinion on the validity of the claim, such as:—

"Mr. A.B. is suffering from a strained back which renders him unfit for work. He states that he sustained this injury lifting a heavy box at work, and in my opinion his condition is consistent with such an accident".

For *disability due to disease*, a medical examination is always required and the patient is referred to an Examining Medical Practitioner appointed under the Act. These appointments have been largely drawn from the ranks of the examining factory surgeons under the old Workmen's Compensation Acts. For the purpose of determining claims and assessing disability, medical boards and medical appeal tribunals have been established, and any doctor interested in such work may apply to serve on these.

This Act is administered by the Minister of National Insurance.

THE DISABLED PERSONS (EMPLOYMENT) ACT, 1944

This Act introduces a new type of legislation, for the preamble states that it is "an Act to make better provision for enabling persons handicapped by disablement to secure employment, or work on their own account".

A disabled person is one who, by reason of "injury, disease or congenital deformity" which may be physical or mental, is "substantially handicapped" in obtaining or keeping employment suited to his age, experience and qualifications. There are no restrictions as to the cause of the disability, and any individual, provided he or she satisfies the requirements of the Act, may apply for registration.

The Act provides for the establishment of vocational training, a register of the disabled, a quota on industry, a list of occupations reserved for the disabled (at present only two such have been designated: car park attendants and electric passenger lift attendants), special factories—"Remploy Factories"—for the employment of the severely disabled, and a National Advisory Council on the Disabled. Of these, the medical practitioner is concerned only with the Disabled Register. Admission to the register is voluntary and is automatic in the case of persons receiving war disability pensions; others may be required to provide medical evidence that the disability is substantial and is likely to continue for at least six months from the time of registration, if it is not permanent. No applications are entertained under the age of sixteen.

Applications are made in the first instance to the local office of the Ministry of Labour and National Service and doubtful cases are referred for medical examination. The prescribed form provided for the medical report, Form D.P.I., is drawn up in such a way that the collated information

allows the disablement to be assessed on a functional rather than on an anatomical basis. The data are also presented in terms which can readily be understood by the layman. This is important, for it is the duty of the Disablement Resettlement Officer of the Ministry of Labour, who has no specialized medical knowledge, to match up the capacity of the disabled person with the physical and mental requirements of different types of work, and ultimately to place that person in a suitable job. A doctor may be asked to advise whether a patient should apply for registration, and it is well to bear in mind certain aspects of the scheme when replying to such a request.

At present just over 900,000 persons are registered as disabled, of whom all but some 75,000 are in employment. At the same time as the original Bill was drawn up it was estimated that about 2,000,000 people would be eligible for admission to the Register, and the fact that only about half that number has actually registered does not necessarily mean that the early estimate was 100 per cent. wide of the mark. It is much more likely that there is still a large number of people who, for some reason or other, have not yet found it necessary to apply for registration or who have some prejudice against so doing. We do not yet know the size of the problem. At the same time it seems that some have found their way on to the Register who really have no right to be there, but this is not surprising in a scheme which is still undergoing its teething troubles. Nevertheless, each one of the 900,000 is an individual problem which the Ministry of Labour has set itself to solve, and it would be a pity if the Register were to become loaded with persons who are capable of fending for themselves in the open labour market. If the phrase "substantially handicapped" is borne in mind when recommendations for registration are made, only those whose disability is serious and who really need assistance will be accepted, and the saturation point of industry will not be so quickly reached. For example, a request to an employer that a patient's occupation be changed should not necessarily carry with it a recommendation that he should apply for registration as a disabled person.

The quota on industry stands at present at 3 per cent. This means that where twenty or more persons are employed in any sort of work, 3 per cent. must be registered disabled persons. For this reason alone it is desirable that only the genuinely disabled should be admitted to the Register.

CONCLUSIONS

Legislation now reaches out into most fields of man's activity and governs many of his daily actions. The average citizen, however, does not appreciate the diverse statutory advantages to which he may be entitled and it is to his doctor that he may turn for advice in these matters, as in so many others. The practitioner may well find it worth while to become acquainted with the elements of social legislation, for this enters into all branches of his professional life and has a close bearing on the health and well-being of his patients.

EPILEPSY AND ELECTRO-ENCEPHALOGRAPHY

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EPILEPTIC seizures and distorted brain waves are inextricably bound together. The epileptic, more than any other group of patients, is the chief beneficiary of electro-encephalography. However, recorded brain waves bear a subordinate relationship to clinical manifestations. What the patient does during a fit merits first consideration. The brain waves may provide either positive or negative evidence which, like laboratory tests in other diseases, can be used by the experienced physician in supporting or not supporting an opinion formed from the history and the clinical examination.

A further reservation applies to the technique of electro-encephalography. The apparatus must be dependable, and the persons who make and interpret the records must be experienced. Such quality work is not unduly expensive. Given four or five patients a day, a five dollar fee should cover all expenses. When the cost is placed against the saving that may result from a possible avoidance of a "work-up" in the hospital, and the even greater money value of proper diagnosis and treatment, the cost of this examination is small indeed. Just as the action of the brain is more intricate than that of the heart, electro-encephalography is more complicated and revealing than electrocardiography. Its rôle in the study of neurophysiology will not be dealt with here. Most laboratories now use apparatus that permits six or eight simultaneous tracings from various areas of the head. Electrodes are pasted to the scalp—a routine recording is for twenty minutes. Deflections of the recording pens are measured in millionths of a volt. Paper speed is three centimetres per second. Important points concern the frequency of the waves (the number of deflections per second), their amplitude, and the wave form or pattern.

DIFFERENTIAL DIAGNOSIS

"Epilepsy" is the Greek word for Anglo-Saxon "fits". Fits may take many forms. Definitions and limitations vary with the philosophy or the experience of the doctor or the writer who uses the term. However, for practical clinical purposes, the diagnosis of epilepsy is one of exclusion. Careful consideration of the details of the fit, plus the surrounding circumstances and the family and past history of the patient, ordinarily permit the separation from epilepsy of conditions such as syncope, carotid sinus syndrome, hypoglycæmic reaction, hysteria, and eclampsia.

Approximately 75 or 80 per cent. of electro-encephalograms made routinely in persons believed to be epileptic display some degree of abnormality, whereas this proportion is only about 15 per cent. in persons

without a history of seizures. Unlike some laboratory tests, the electro-encephalogram does not give a simple plus or minus answer, but presents many degrees of abnormality and specificity. Thus, records containing seizure discharges (high voltage waves that are abnormally fast or slow) occur in about 40 per cent. of epileptics during a 20-minute recording. They are approximately forty times more numerous in epileptics than in non-epileptic normal persons. A background rhythm that is far outside the bounds for the normal adult of from eight-and-a-half to twelve waves per second, is thirteen times more frequent; whereas a background rhythm only a little outside this normal range is only twice as frequent in epileptics as in "normals". The types of abnormality and their relative incidence in a normal and an epileptic adult population are shown in the accompanying figure which is a modification of the Gibbs' (1943) classification (fig. 1). These recordings were made in interparoxysmal periods. In England, Williams (1944) has compared the findings in epileptics, normals, neurotics, and persons with open and closed head injuries.

The electro-encephalogram may therefore support with varying degrees of certainty a diagnosis of epilepsy made on clinical grounds, or it may provide no support. Lack of support in no way invalidates a clinical diagnosis of epilepsy. "Normal" records are especially common in patients whose seizures have been few or separated by long intervals of time. The electro-encephalographer may report that the tracing contains seizure discharges and is confirmatory of epilepsy, or that variations from the normal are moderate and the record is merely suggestive of epilepsy. Borderline abnormalities carry little weight. Another difficulty is that, unlike some laboratory tests, the brain waves are a fluid characteristic and, even more than the electrocardiographic abnormalities, their degree may vary from day to day and may change with alteration in the activity of the brain, and in the chemistry of the blood flowing through it. Also, waves tend to become faster and abnormalities less prominent as persons grow older. Changes with age are especially pronounced up to and through puberty. Hence, electro-encephalograms of children are more revealing, but also more difficult to interpret than recordings of adults.

CLASSIFICATION OF SEIZURES

Fits can be divided into three main groups. On the basis of symptomatology, these are: First, convulsions (*grand mal*). Convulsive seizures may be separated into those with bilateral generalized movements, those that are one-sided or localized, and finally those with a march of movement or sensation (Jacksonian or Rolandic seizures). Second is the *petit mal* triad (Lennox, 1945), consisting of *petit absence* (or pyknolepsy), myoclonic jerks, and akinetic (drop) seizures. Third are psychical seizures, including such diverse manifestations as automatism, tonicity with chewing or swallowing motions, mania, dream states, hallucinations and simple amnesia. However, many seizures, especially in children, cannot be thrust into any of these

three pigeon-holes; for example, prolonged faint-like episodes, breath-holding spells, autonomic seizures and abdominal epilepsy.

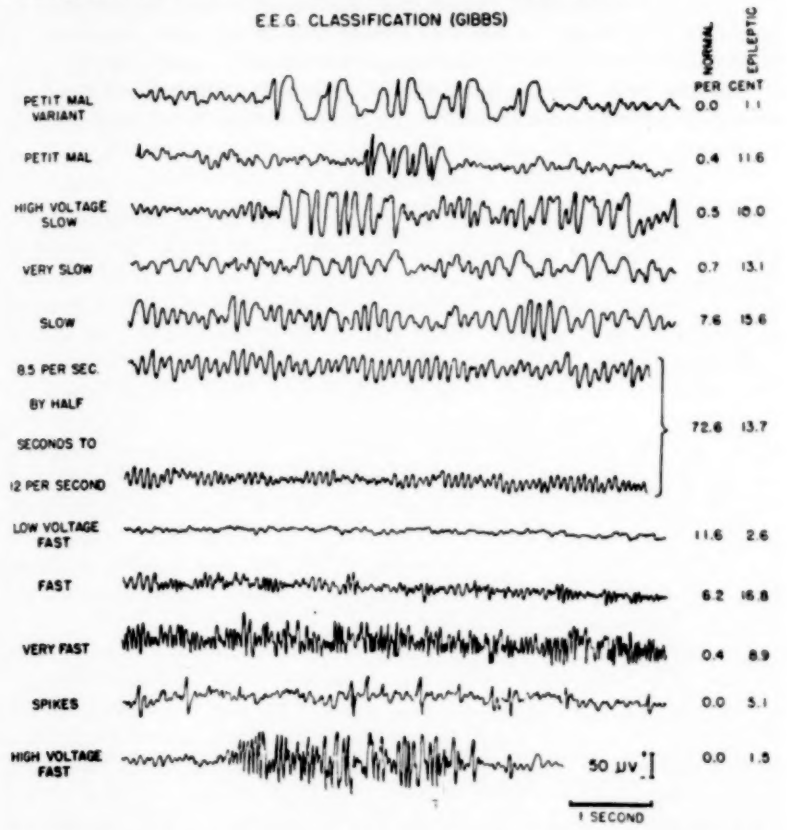

Fig. 1.—Classification of the electro-encephalogram used by the Gibbs. The upper three and the bottom two tracings illustrate seizure discharges. The tracings central to these illustrate dominant frequencies which are either slow or fast. Frequencies of from 8½ to 12 per second, and those marked low voltage fast, are considered normal. The signal at the bottom line marks a deflection caused by 50 microvolts, and the horizontal line, one second of time. At the right is the distribution of each type of record found in 1000 control adults and in 730 adult epileptics.

Electro-encephalograms made during a seizure are broadly distinctive: high voltage sharp spikes at the onset of a convulsion, high voltage slow waves during an automatism, and high voltage alternate fast and slow (dart and dome) waves recurring at a rate of three per second during a *petit absence*. Were it not for the electro-encephalogram, a *petit absence* status lasting for many minutes, or even hours, might be indistinguishable from mental confusion and amnesia characterizing a psychical seizure.

In inter-seizure periods, the most suggestive findings are fragments of

the dart-dome series in patients subject to *petit mal*, or solitary spikes over a temporal lobe of those subject to psychomotor attacks. These two electrical phenomena, but especially the alternate dart-dome discharges, are the only wave forms that may be considered of diagnostic significance. Localized foci of abnormality may be associated with localized convulsions. A given patient may have differing types of seizures, and in most patients the inter-seizure recording does not identify the seizure pattern to which the person is subject.

ETIOLOGY

The two main causes of seizures are: genetic (idiopathic, essential or cryptogenic), and acquired (symptomatic). In favour of the former is a history of fits or of migraine in some blood relative, or demonstration of disturbed brain waves (not an acquired condition) in a parent. In favour of an acquired epilepsy is a history of brain injury that antedated the first seizure, such as a difficult delivery, early spasms or periods of limpness or cyanosis, or in later life evidence of encephalitis or brain injury, brain tumour, and so on. Genetic and acquired sources of seizures are not mutually exclusive. In a survey of 1,200 private patients, we obtained a family history of epilepsy or migraine in 33 per cent., evidence of gross brain injury in 15 per cent., and both of these two conditions in 8 per cent. In the remaining 44 per cent., neither genetic nor acquired factors were elicited. These might be called the true cryptogenic cases, but experience shows that this number decreases progressively with increasing completeness of family or past histories, and with thoroughness of examinations.

The electro-encephalogram may help to distinguish genetic from acquired epilepsy. The brain-wave tracing is an hereditary trait. Identical twins have records that are indistinguishable and, if one of the pair is epileptic, without antecedent brain injury, the co-twin is almost certain to experience the same type of seizure and display the same abnormal wave pattern in his electro-encephalogram. Theoretically at least, help might be gleaned from records made of the parents, a procedure that is seldom feasible. An electro-encephalogram of the patient showing dysrhythmia that is generalized and symmetrical, especially if the pattern is three per second dart and dome, favours genetic epilepsy. Foci of abnormality, especially if composed of spikes or very large slow waves, favour an acquired epilepsy, the result of localized brain pathology. Of course, the electro-encephalographic record must be interpreted in the light of the patient's history. Localized injury may be the result rather than the cause of the first seizure.

The electro-encephalogram may conceivably be of use in advising patients about marriage and children. Marriage of a genetic epileptic seems to be especially hazardous if the intended spouse is found to have a diffusely abnormal record.

PROGNOSIS

For patients, this subject is paramount in importance. In former decades,

genetic epilepsy, almost by definition, was regarded as a progressive disease, seizures becoming increasingly frequent and severe, and the mentality progressively lower. Now it is realized that, failing the presence of gross brain pathology, the natural tendency is for brain waves to become more stabilized and seizures to become fewer with advancing years. However, the greatest differences exist. Although prophecy is dangerous, certain broad predictions can be made on the basis of the history and clinical observations. Any brain damage sufficient to cause neurological signs reduces the chances of recovery and makes control by means of medicine more difficult. Convulsions that are frequent, prolonged and severe, endanger the future because of possible resulting brain pathology. The outlook for psychomotor seizures may be more grim than the relative mildness of attacks would suggest. Generalized convulsions are usually preferable, in that spontaneous remission or cessation of attacks occurs more often with convulsive than with psychical seizures. Spontaneous cessation of attacks and the associated dysrhythmia are especially frequent with patients having ***petit absence***, a form that tends to die along with attainment of adulthood.

Because of the urgency of the question and the uncertainty of the answer, any help that the electro-encephalogram can give is doubly welcomed. Confirmation of the clinical diagnosis of the ***petit mal*** triad, through demonstration of alternate three per second spike-wave discharges in the electro-encephalogram, is a favourable finding. However, if these discharges should be of the slower, two per second type, the prognosis is clouded, because such formations are likely to be based on brain pathology. The degree of abnormality, as shown by the proportion of the total record dominated by slow spike-wave complexes, may not coincide with the severity of seizures as judged clinically. Thus, a person with a history of only a few attacks may yet have an extremely abnormal record, and *vice versa*. Also, localized spike or slow wave discharges may suggest localized brain injury when neurological signs are absent. Persistent convulsions that show little response to attempted restraint by medicines may occur in a patient with a perfectly normal record, but in general a normal appearing record, especially if this is found on repeated occasions, is a basis for a relatively good prognosis. Conversely, much instability of the background frequency of waves, much slow activity or many seizure discharges, call for caution regarding the eventual outcome, even when seizures are few or their initial response to treatment is favourable. Although the electro-encephalogram is in no sense a measure of intelligence, much abnormal slowing or many localized spike or slow spike-wave discharges, suggest a poor outlook for mentality, probably because of the damage to the brain which the abnormalities suggest.

TREATMENT

Clinical experience dictates the form treatment should take. A history of localized brain trauma, Jacksonian or focal convulsions, one-sided neuro-

logical signs, lateralized abnormality of a ventricle after insufflation of air into the ventricles or subarachnoid spaces—such evidence points to localized pathology. If the history and the examinations point to an area that can be reached by operation, exploration with a view to possible excision of the offending area is in order. Waves from electrodes applied to the scalp often point to the approximate area to be exposed. More important than removal of scar tissue is the excision of the gyrus or gyri from which the abnormal waves arise—the epileptogenic focus. For the identification of such a focus, electrodes are applied to the cortex at the operating table, and various points on the cortex are stimulated with a weak current. A point which "fires" is judged to be the guilty area. Excision of tissue of a temporal lobe which contains a spike focus in patients subject to psychic or psychomotor seizures is a logical procedure, but the ultimate value has not yet been determined.

In *medical treatment*, convulsions are best controlled by one or possibly a combination of two of the well-recognized anticonvulsants; namely, phenobarbitone (luminal), phenytoin sodium (dilantin sodium or epanutin), methylphenylethylhydantoin (mesantoin). These drugs, preferably singly, but if necessary in combination, are given with gradual stepping up of dose until either attacks are fully controlled or toxic symptoms appear. Psychomotor seizures are controlled with more difficulty. Dilantin or mesantoin, or a combination of these, gives greatest hope of success. A new drug, phenacetylurea (phenurone), resulted in benefit in nearly one-half of our cases when all other remedies had failed. It may also benefit *petit mal* and convulsions. However, phenurone is not on the market and may not be if present suspicion of a toxic effect on the liver should be confirmed. For members of the *petit mal* triad, trimethyloxazolidine dione (tridione) or dimethylethyloxazolidine dione (paradione) is the drug of choice (Lennox, 1945).

Successful therapy presupposes adequate dosage. The amount that patients can tolerate is highly individual. For most patients, symptoms of toxicity appear at about the following dosage: phenobarbitone, 0.3 g. (5 grains); diphenylhydantoin, 0.6 g. (9 grains); methylphenylethylhydantoin, 0.9 g. (12 grains); tridione and paradione, 1.8 g. (28 grains). Success of therapy also implies conscientious supervision of patients, with change of medicine or of dosage when indicated, and early detection of unpleasant or dangerous side-effects. Drowsiness may attend larger amounts of phenobarbitone or mesantoin. Rash may be an allergic response to mesantoin, epanutin, tridione or paradione. Photophobia may accompany the last two, and muscular incoordination or swelling of gums may result from phenytoin sodium. More serious is an aplastic anæmia that has occurred in several patients taking either tridione or mesantoin. For this reason, there must be monthly blood examinations, with discontinuance of the medicine if neutrophils fall below 1,600 per c.mm. or if platelets are diminished.

The electro-encephalogram, by confirming a diagnosis of *petit mal* with its spike-wave discharges, strengthens the decision for choice of tridione or

paradione. Temporal lobe spike discharges, often obtained only during sleep, speak for dilantin or phenurone. Otherwise, the electro-encephalogram does not give specific advice about medicines to be used. However, it often helps to decide about the termination of treatment. The improvement of seizures and of the brain waves do not necessarily follow a parallel course, but ordinarily they do—the improvement in the tracing lagging behind the improvement in the seizures. Discontinuance of medication seems safer if the brain-wave tracing has improved to the point of being normal or nearly normal. Successive recordings may be helpful also in social therapy. A normal or relatively normal record encourages a relatively constructive programme for education and training for employment. The case for institutionalization is strengthened by an electro-encephalogram profoundly dysrhythmic, with predominance of waves that are grossly slowed or are of the slow spike-wave type.

CONCLUSION

Clearly, physicians are much better able to cope with epilepsy than they were ten or fifteen years ago. This improved outlook is due in large measure to information furnished by the electro-encephalograph and to the therapeutic efficacy of newer drugs. Both are the outgrowth of persistent medical research. Practitioners who wish to keep abreast of new knowledge and new treatments may consult the international periodicals: *Journal of Electro-encephalography and Clinical Neurophysiology* and *Epilepsia*, or join the International League Against Epilepsy, of which Macdonald Critchley of London is President. The "Atlas of Electro-encephalography", by F. A. and E. L. Gibbs, has been the standard work on that subject, but is being superseded by a new edition.

However, much needs to be learned about the origin of seizures, and even better chemical therapy must, and can be, developed. In general, social therapy has lagged far behind medical and surgical treatment. The value of seizure control is in large part cancelled if the victim is denied opportunity to learn and to work because he has had seizures. The public must be educated away from present misconceptions and prejudices, and epileptics must be given increased opportunities for education, training and employment.

Thanks to electro-encephalography and newer drug therapy, epilepsy need no longer be considered inscrutable and incurable. Given experienced and conscientious medical attention, most patients can be relieved of the majority of their seizures and some may attain complete, and possibly permanent, relief.

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OBESITY AND ITS TREATMENT

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An increase in weight is always due to eating more than the body requires; it depends therefore upon an appetite disproportionate to the body's needs. Fat people are often ashamed of their obesity and, because they fear to be accused of gluttony, prefer to assume they are suffering from some abnormality in their metabolism. There is, however, no evidence that the obese utilize food differently from the spare, or that they have superior absorptive powers which enable them to extract the last calorie from their food. Investigation of the stools of subjects on standard diets shows that there is no difference between the fat and the thin in their ability to absorb food; whilst studies of nitrogen metabolism in the two groups demonstrate that their metabolic requirements follow the same rules. In fact, the total metabolic requirements of the obese are considerably greater than those of the thin, and a moderately fat person may require as much as 25 per cent. more calories under basal conditions than he would were he his ideal weight. Such extra energy is needed to maintain his excess tissue and to allow for increased loss of heat due to an increased surface area.

APPETITE

As the metabolic laws are identical in the thin and the fat, and as, indeed, the basal metabolism of an obese person actually exceeds his ideal requirements, it follows that a fat person is one who has eaten too much; too much, that is, in relation to his total energy requirements, which may be separated into his basal needs and his needs due to whatever external work he does.

It is remarkable how constant a person's weight remains over long periods and how exactly the appetite is related to bodily requirements so that, in health, the weight is maintained within a pound or two. Even during periods of increasing weight, the rate of increase may be small. It is clear that there must be some very nicely adjusted physiological mechanism by which the appetite controls the quantity of food ingested. There must be some upset in this adjustment in the obese, so that a feeling of satiety is not reached until more food has been eaten than is required for the work the body does. It is not certain how this adjustment between appetite and metabolic needs is made. It has, however, been suggested that the feeling of satiety following a meal depends upon the increase in skin temperature which follows it, or, perhaps, the rate of increase. Thus persons of normal weight can eat no more after the skin temperature has risen 0.9°C. in 22 minutes. In the obese, on the other hand, the rate of increase of temperature is slower, so that the level at which satiety is attained is not reached and more food is therefore desired (Evans, 1947).

How far such differences of rate of heat production are constitutionally determined, and how far they are results of having become thin or fat in the first place from other causes, it is difficult to say. It may well be that the beginnings of obesity may lie in example and in opportunity and, once the preliminary layer of fat is laid on, diminished heat production leads to a further enhancement of appetite; so a vicious circle comes about.

ENDOCRINE DISORDER

Because certain endocrine disorders are associated with obesity, it is tempting to ascribe the accumulation of fat to glandular upset. Although obesity is seen in eunuchism, certain pituitary and hypothalamic disorders and, indeed, in other brain diseases, and also in myxœdema, the relation is less direct than might be supposed. More often when there is a disturbance of fat metabolism, the weight is not much increased but the fat of the body is peculiarly distributed; for example, in Cushing's syndrome, the weight is about the trunk whilst the extremities remain spare. Eunuchism is not necessarily associated with general increase in weight; nor is myxœdema (Greene, 1948).

Although obesity may be associated with these endocrine disorders, it is incidental to the general state. No endocrine preparation is of value in the treatment of obesity as such, and diminution of an "endocrine" obesity following specific treatment will only occur if attention be paid also to diminishing the intake of food to a quantity commensurate with the energy output.

THE METABOLIC EQUATION

Whatever other problems obtrude, we cannot escape from the metabolic equation which applies equally to the fat, the "ideal" and the lean.

$$\begin{matrix}\text{INTAKE}\\ \text{OF}\\ \text{FOOD}\end{matrix} = \begin{matrix}\text{BASAL}\\ \text{REQUIREMENTS}\end{matrix} + \left\{\begin{matrix}\text{ENERGY REQUIRED}\\ \text{FOR}\\ \text{EXTERNAL WORK}\end{matrix}\right\} + \begin{matrix}\text{WEIGHT INCREASE}\\ \text{OR}\\ \text{WEIGHT LOSS}\end{matrix}$$

It is evident from this that any treatment designed to decrease a person's weight must be directed towards some alteration in one of these variables.

No patient wants to reduce the amount he eats, because the amount he eats is the quantity he needs to attain the pleasant sensation of satiety. It would therefore be convenient to find some means of diminishing the appetite. Lesses and Myerson (1938) first introduced amphetamine for this purpose, and *d*-amphetamine is now sometimes used and may be given in doses of 5 mg., three times a day before meals (Colton *et al.*, 1943). It is undesirable in patients who are hypertensive, and fat people often are, whilst in any patient its continued use is undesirable. I doubt whether it is of much value in treatment, as the only effective physiological way to reduce the appetite is by diet and re-education.

It would be more in accord with the patient's desires if the number of calories he uses could be increased; but it has already been shown that the basal requirements of an obese person are considerably greater than they

would be if he were his ideal weight. An increase in the basal metabolic rate has, however, formed the basis of the treatment of obesity with thyroid extracts, which, incidentally, is the only endocrine preparation that will in itself cause a reduction in weight. Any measurable effect can only be obtained by giving the patient sufficient extract to make him ill with thyrotoxicosis. The exception is, of course, when the obesity is definitely related to thyroid deficiency, a condition seen most often in women about the time of the menopause.

Other drugs, the dinitrophenols, have been used to increase the metabolic rate; this they do, but as they also cause cataract and death, their use has properly been abandoned.

The next variable one might consider changing is the external work done. This is usually impracticable and almost always undesirable. Obese subjects are not accustomed to physical exercise, and only very considerable physical exertion will be effective in producing any loss of weight. Apart from the strain of such exercise on a probably weakened myocardium, the enhancement of appetite which occurs more than outweighs any advantages which might be gained. If therefore it is undesirable to increase the basal metabolic rate, and impracticable as well as undesirable to increase the external work done, it follows that the only practical and, indeed, practicable method of treating obesity is to reduce the amount of food eaten.

WATER RETENTION

Water retention plays an important contributory part in determining the gross weight of a fat person. Adipose tissue holds much water, and it has been suggested (Greene, 1950) that water retention might sometimes be the basic disorder and that fatty tissue is therefore laid down as an essential corollary to this.

THE DANGERS OF OBESITY

The dangers of obesity are very real and they must be appreciated by the patient as well as by the physician. Insurance companies are well aware that an increase in weight of more than 10 per cent. above the "ideal weight" is associated with a reduction in the expectation of life, and the risk increases rapidly as the weight soars.

In the really obese, diabetes mellitus is much more common than in the thin, and, indeed, an obese diabetic taking large quantities of insulin may regain an almost normal tolerance for glucose following effective reduction in weight. The degenerative diseases, especially myocardial and arterial degeneration, are much greater risks in the obese. Even the suicide rate is higher in the really fat than in the thin. Among the important causes of death, only from pulmonary tuberculosis do the obese enjoy a relative immunity.

THE TREATMENT OF OBESITY

Because the whole basis of treatment lies in dietetic restriction, any attempt

in weight reduction can only be effective with the patient's full cooperation. For this reason it is essential at the outset that he should know how his weight is to be reduced and also why reduction, apart from æsthetic and cosmetic reasons, is desirable. It is useful therefore to tell him something of the dangers which go hand in hand with excessive weight. He should also understand that his excessive weight is due to excessive eating. It is usual for any suggestion of gluttony to be strenuously denied, and it may well be true that the patient has indeed not eaten an excessive bulk of food. It must be pointed out that a small meal in bulk is not necessarily a small meal in calories, and that it will be possible, by a careful choice of food, to see that he still can get a satisfying large meal, at any rate in appearance.

It is best to treat the patient in bed to begin with; appetite is lessened and stricter discipline can be imposed. He should be weighed daily and given a fixed diet similar to the "Strict Anti-Fat Diet" drawn up below. There is no need for the patient to fast entirely, nor to be restricted beyond the limits of this diet, for excessive reduction in diet leads to irritability and often, too soon, to a refusal of the patient to endure further treatment. The diet, in spite of its not unsatisfying appearance, does not provide more than about 60 grammes of carbohydrate and 10 grammes of fat. The difficulty with present rations is to provide enough protein as meat, but by the use of readily available unrationed fish, rabbit and game, the diet should contain about 70 grammes of proteins a day or more. This brings its calorific value to the region of between 600 and 700.

STRICT ANTI-FAT DIET*
(For Reduction in Weight)

Breakfast
Half a grapefruit.
Two small pieces of toast with *thin* spread of unsweetened marmalade.
Tea (with lemon and saccharine), or coffee with saccharine and 1 oz. of milk.

Luncheon
Lean meat (beef, mutton) or one of the following fish: haddock, cod, whiting, brill, sole or plaice, not fried; or chicken or game.
Any of the following green vegetables: spinach, vegetable marrow, celery, brussels sprouts, asparagus, cauliflower, cabbage, leeks. No extra salt.
Pickles, or salad; lettuce, watercress, cucumber, radishes, celery, tomatoes; with vinegar, as little salt as possible and no oil.
Jelly. Bottled unsweetened fruit. No pudding.
One biscuit (or toast Melba).
Black coffee with saccharine.

Tea
One or two cups of tea with lemon and no sugar.

Dinner
The same as luncheon.

It is important that no extra salt be taken other than that used in cooking, in order to facilitate the excretion of water. Similarly, the fluid intake may be reduced to two pints a day and the use of a mercurial diuretic is often very helpful. Although the amount of water retained in the body will eventually

*From the Guy's Hospital Pharmacopœia.

adjust itself to the reduced quantity of adipose tissue, it is encouraging to the patient if he can see some unequivocal loss of weight in the first week or two, to recompense him for his privations. For this reason, in the absence of any contraindications, it is useful to give an injection of 2 ml. of mersalyl every four days after a preliminary test to exclude idiosyncracy. With such measures it should be possible to lose ten pounds (4.5 kg.) in the first fortnight of treatment.

Ideally, treatment in bed should be continued until the desired weight is attained, but often this is not possible. It is difficult for a patient to remain on a very low diet when he is working without feeling uncomfortably hungry and fatigued, and then he will often succumb to the temptations of the larder. However, once the desired weight is reached, it is not difficult to keep it at that figure, and he may then follow the maintenance diet.

ANTI-FAT DIET*

(For Maintenance)

Avoid sugar; saccharine may be used as a substitute.
,, potatoes, turnips, beetroot, parsnips, peas and onions.
,, salmon, turbot, herrings, mackerel, sardines.
,, pork and ham.
,, cream.
,, bread with lunch and dinner.
Take no second helpings.
Take no food apart from breakfast, luncheon, tea and dinner or supper.
Take plenty of green vegetables, salads (without oil) and clear soup.
Alcohol in all forms should be avoided.

The value of salads, fruits and clear soups in providing bulk to the meal should be specially stated. Any increase in weight should be followed by resumption of the strict diet, and many patients find it quite tolerable to have one "fast day" a week during which they take only fruit and salads. In older patients, and especially in those who have shown evidence of myocardial disease, this may be combined with a day resting largely in bed.

The patient who has rigidly followed this regimen, may well keep to it indefinitely because of his increased energy and sense of well-being. But there will be many to whom the pleasures of the table remain too great a temptation. They must make their own choice.

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ASTHMA IN CHILDHOOD

AN UNSCIENTIFIC EXPERIMENT

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When inquiring into the history of asthmatic children no one can fail to be struck by the frequency with which the mothers say that excitement brings on the asthma—"he works himself up whenever he is looking forward to anything, then has asthma and can't do it" or "she always gets it when she is going to a party".

Christmas seemed to us a suitable time to test the truth of these statements. We therefore organized a party for the sixty children who had been attending the Play Clinic at the hospital during the previous two years. (Briefly, this Clinic had been started to assess the children's background, to give advice to mothers, to give communal breathing exercises, and to observe the children in their relation to others of their own age (Clarke, *The Practitioner*, 1949, **163**, 130).)

Every effort was made to see that our party was a good one, and to stimulate as much anticipation and excitement as possible. Proper invitations were sent out, constant reminders were given, and the party discussed for weeks beforehand. On the actual day the room was decorated and Father Christmas came to give out presents. The children burst innumerable balloons, blew whistles and lit the Christmas tree. After eating an enormous tea they rushed about playing excitedly. In most cases the mothers were with the children in the background.

Sixty-nine children were asked to the party, and of these forty-six accepted. Fourteen refused for reasons other than asthma (mostly on account of distance), and nine did not answer. Of the forty-six who accepted, four were unable to come because of attacks of asthma, but in none of these cases was excitement listed as a "cause" by the mothers. Forty-two children therefore came to the party, and of these twenty were specifically stated to get asthma when they were excited or looking forward to anything. In fact only two of these wheezed at all—and that very slightly—the remaining eighteen being entirely well, before, during and after the party. Those whose asthma was ascribed to different causes were also perfectly well. Taking the party as a whole we thought the children behaved entirely normally and that four absentees out of forty-six acceptances was not an unusual figure for any party.

DISCUSSION

There seem to be several possible reasons why attacks of asthma were not precipitated. First, the history given by the mothers may have been ex-

aggerated or even untrue, but the statements were made so often and so spontaneously that we think this is unlikely. Secondly, the children may already have been vastly improved by their treatment (in some cases this was undoubtedly so), but we found there was no direct relationship between the length of the treatment and the state of well-being, since many of the children were new patients. A third possibility is that the children did not consider it a normal party because it was at the hospital. This is difficult to disprove, but there was no doubt of the party's success, and the tension beforehand was considerable, the children clamouring at the door before we were ready for them. They were also all dressed up in their best clothes and after getting over their initial shyness they were full of excitement all afternoon. A fourth possibility is that the *mothers* regarded it as "something different", and this on the whole we think most likely. There would not be so much maternal solicitude over keeping the child well as if he were being sent among normal children. In general, we think our party involved much less maternal strain and gave little cause for over-protection; in particular the mother knew that if the child did break down in any way it would not matter.

Since starting to investigate asthma we have been impressed on the whole by the trivial nature of the exciting causes. If this be true we might expect to find also that trivial changes would often effect improvement. This we believe to be the case. A slight alteration of environment, a new drug, avoidance of a heavy meal, or even nothing more than an investigation may bring about a remission. When, as is often the case, the cause of the improvement is inexplicable, the alteration may be too small to be appreciated by patient or doctor. In our particular case a slight alteration in the party background appears to have been enough to prevent attacks. We feel that we had unwittingly influenced the child and his mother to look forward to the party in a more normal way. Stability of background is, we feel sure, the most important single factor in the treatment of asthma in childhood, and we feel that our experiment helps to show that attention to detail in this respect is of considerable importance.

CONCLUSIONS

(1) The reactions of forty-two asthmatic children to a Christmas party are described.

(2) In twenty of these children the mothers specifically stated that excitement and "going to a party" brought on asthmatic attacks. In none of these twenty children was asthma precipitated by the party described, although two wheezed slightly.

(3) The significance of this is discussed, and the most likely explanation is the absence of *parental* tension or excitement in the given circumstances.

(4) A possible bearing of the above on the treatment of asthma generally is suggested.

EMERGENCY BED SERVICE

A SERVICE FOR THE GENERAL PRACTITIONER

By R. E. PEERS

Secretary, Emergency Bed Service, King Edward's Hospital Fund for London.

In 1937 the Voluntary Hospitals Committee for London considered a proposal made by Mr. A. J. Gardham, F.R.C.S., to devise a system which would relieve the general practitioner from the waste of time involved in finding a hospital bed for a patient. Doctors complained that they were often called upon to spend hours telephoning to one hospital after another in order to find a bed. A deputation from the Voluntary Hospitals Committee laid the problem before King Edward's Hospital Fund, and it was agreed that an admissions office should be set up by the Fund at its own expense.

The service was started on June 21, 1938, in the King's Fund offices in Old Jewry. The staff was entirely non-medical. Their duty was to record the necessary details of the case which the doctor would supply over the telephone, and find a bed in a hospital either of the doctor's choice or of their own discretion, as the doctor might think fit. To assist them, daily statements of vacant beds were obtained from all major voluntary hospitals. The system worked satisfactorily and the new service was warmly welcomed by doctors. In 1938 it seldom took more than twenty minutes to find a bed, call an ambulance and advise the doctor of what had been done. For every case admitted an average of 1.4 hospitals were asked to admit. On the first day open, seven doctors rang up, but by midsummer 1939 over 7000 cases had been dealt with. About the same number were dealt with in the month of January, 1950.

The war, or to be more precise the Emergency Medical Service, rendered the work of the service almost redundant, and only 2000 or 3000 cases were dealt with in each war year, the number being in inverse ratio to the German air activity.

FUNCTION UNDER THE NATIONAL HEALTH SERVICE

With the end of the war the use of the service began to increase rapidly, and by 1948 it was receiving some 15,000 cases a year. Meanwhile, soon after the passing of the National Health Service Act the Ministry of Health asked the service to be prepared to deal with all urgent admissions for the four Metropolitan Regions. When the Regions were established, arrangements were made for the King's Fund to continue to run the service as agent for the four Metropolitan Regional Hospital Boards, the Boards to pay the whole of the additional costs. The service then became responsible for the admission to hospital of all urgent cases, including infectious diseases, with which it had not previously dealt, but excluding tuberculosis and mental cases. This made a fundamental alteration to the status of the service. Hitherto it had been a voluntary organization which could admit to failure,

but, under the new order, failure to find a bed might keep the patient out of hospital altogether. Clearly a lay organization could not carry such a responsibility, and in consequence two doctors employed by the Boards jointly have been attached to the service permanently in order that they can bring the Boards' authority to bear if a bed cannot otherwise be found for a really urgent case. Alternatively, if the case is not sufficiently urgent to warrant putting up an extra bed in an already full hospital, the Board's doctor can authorize the service to abandon the case. This was worked out before the appointed day. What could not be estimated was the increase in the volume of the work. Various calculations were made and finally it was decided to anticipate a 100 per cent. increase, and staff was appointed and trained accordingly. At the same time advice on the management of an Admissions Service for urgent cases was given to nearly all the new Regional Boards.

July 5 came, and I went to the office wondering whether the new Health Service would have made some tremendous difference to the work, or whether, as so often occurs in a foreseen crisis, nothing much would happen. Everything happened. From one day to the next the work went up 400 per cent. and beds became much harder to find. Part of this was a general increase in work due to shifting of the duty to admit patients from the Council hospitals individually to the Health Service as a whole. Partly also it appeared to be due to a desire to embarrass the Health Service on the part of some ardent opponents. That chaos did not ensue was due to the devotion of the staff. The "backroom" staff (they were only three) were called into the operations room, and fortunately the operational staff had previously agreed not to take holidays for six weeks after July 5. By the end of August the pressure fell slightly, the maximum staff that the office space and equipment could carry had been appointed, and they were coming into use as fast as they could be trained. This restored the situation temporarily but it was evident that the staff would be heavily overloaded in the winter and, since there was too little time to take and equip new offices, it was decided to carry on and try to improve our technique so that the work would be speeded up. The monthly total of applications had been 1,155 in June, then rose to 4,252 in October, 5,012 in November, 4,907 in December, 5,833 in January, and 5,988 in February; then the wonderful spring of 1949 came to our aid and in March, instead of being higher still as past experience indicated, the total fell to 5,464.

A careful inquest on the winter's work was at once started and it revealed that from the appointed day to the end of April 1949 there had been no means of finding a bed for 4,052 patients out of a total of 45,682. These had nearly all been aged sixty or over. The failure to get these beds, however, lay not with the service, but in the general shortage of beds that has been manifest ever since the war, and has become more acute since the start of the National Health Service. What was to the discredit of the service was the great length of time taken to tell the general practitioner of the fate of his

patient. When the patient had been admitted this time averaged 56 minutes; when he had not got in it was 3 hours 54 minutes. This, by our pre-war record of 20 minutes, was indeed a challenge. It will readily be understood that any serious change in the working of the service has to be made during the summer when the work is at its slackest. One is told never to swap horses in mid-stream, and our stream is in spate in the winter. Spring is planning time, summer is changing time, and in winter comes the test. In April, May and June much careful thought was given to planning for the coming winter. The previous winter's work was analysed, and finally it was decided that the best course open to the service would be to enlarge and decentralize. There was no need to do this before the autumn as we felt sure we could handle the summer load without difficulty. Accordingly, towards the end of the summer new staff was appointed and trained, and in September and October branch offices in Leytonstone, Woolwich, Ealing and Wimbledon were opened, and linked by tie-line to Old Jewry.

WORKING OF THE NEW SCHEME

The branch offices were set up in order that they should take the load off Old Jewry. Their position was chosen after careful search of the areas from which calls came, and it has worked out that one is situated in each of the Metropolitan Regions. They do exactly the same type of work as the head office and cases can be freely interchanged. In practice it has been found that these offices have been more successful in admitting patients in the outer parts of London than has head office. This presumably is because they are in closer touch with the local hospitals. These branch offices are open every day from 8.30 a.m. to 9 p.m. and are housed in hospital premises at Leytonstone (LEY 6461), Ealing (EAL 6671), Wimbledon (WIM 6581), and Woolwich (WOO 3471). Outside these hours calls should be made to Old Jewry (MON 3000). Although the Service is not intended to deal with the admission of chronic cases, it has always been felt that it is better for the Service to accept such cases when offered and place them on the waiting list of the appropriate hospital rather than refuse to help the doctor. All such applications are allocated to waiting lists by the branch offices in order to take the load from the centre.

The efficiency and success of the Service depends upon the staff. Methods of work, returns of bed states, and so on, all have their place, but a good staff is the first essential. Great care is taken in the choice and training of the staff. They must be both pleasant and efficient, good mannered, good tempered, and with a school certificate degree of education. If applicants appear to have these qualifications they are appointed on probation and trained. This involves obtaining a working knowledge of medical terms and their meaning, of the geography of London, and of the whereabouts, capabilities, and even idiosyncracies, of the London Hospitals. We have had the good fortune to have an adequate supply of candidates so that the standard can be maintained.

The London operational staff is now increased to 50 as against 22 before the appointed day. At first sight this may seem a large number of girls to employ, but on remembering that the office is open seven days a week and twenty-four hours a day it will be realized that a large staff is necessary. No statistics are yet available of the resultant increase in the speed of handling cases, but it is evident that in spite of an increase of 26 per cent. in the number of cases in January 1950, as against January 1949, the delays attributable to the service have been considerably reduced. This does not mean that we are back to the 20 minute standard or anything like it. That can only be reached when the supply and demand for beds has reached pre-war standards. The Boards and Hospital Management Committees have been successful in opening a large number of beds during 1949 and we have, in consequence, been able to admit many more patients.

It remains, however, that practitioners often have to wait long to get the service's answer and, since the service was started to eliminate waste of doctors' time, a scheme has been started whereby cases of extreme urgency are guaranteed admission on application to the Regional Board doctors, and the general practitioner need not therefore wait for an answer, as he is certain that his patient will be admitted as soon as possible. Since the war doctors have had a lot to put up with and among their trials has been the deterioration of the service we had given. But we have improved and intend to improve further; meanwhile we hope doctors will be forbearing—"Don't shoot the pianist, he is doing his best!"

THE AGED SICK

Perhaps a footnote may be added, although it is not strictly the work of the E.B.S. The experience of last winter brought out forcibly that part of the hospitals' troubles lay in the number of aged sick who, once in hospital, never go out again. Many of them spend years in hospital, requiring little nursing and getting no better. The King's Fund, being aware of this and having the Service's figures before them, set aside a sum of £250,000 to establish homes for these patients. These homes are to be less heavily staffed than the hospitals, but closely attached to hospitals so that they can take from them the long-stay cases. The geriatrician of the hospital will be the medical officer of the home, and will be able to move patients to and fro as their condition requires. Endless difficulties are being met in setting up these homes. Suitable houses are scarce, town planning, building licences, and the like, involve long delays, but gradually they are coming along, and in due course they should make their contribution to easing the position, and carrying out the Fund's duty to relieve the sick.

THE MECHANISM OF HYPNOTISM

By C. G. LEAROYD, M.R.C.S., L.R.C.P.

In a previous article[1] I have postulated that sleep is caused by an inhibition spreading from the basal ganglia to all the senses in settled sequence, the last-formed going to bed first. The chief characteristic of this mechanism is that the numbing of a sense is preceded by that sense dominating the consciousness, which as the regress takes place has a diminishing scope; the organism is obsessed by the sense that is about to be numbed; excitation of it precedes its narcosis.

Hypnotism is induced by the excitation of one sense to the exclusion of all others. Hypnotic sleep will follow if the suggestion is made or if the "sleep wish" is present, but it is not an essential part of hypnotism. There is no need for a hypnotized person to sleep. The association between hypnotism and sleep is that the upper part of the sleep mechanism is also the mechanism of hypnotism. Braid tried to recall his word "hypnotism" because he realized that sleep is not an essential part of it. Nearly everybody is hypnotizable except psychotics. Erickson says that any really cooperative subject may be hypnotized. With each hypnosis the process becomes more easy, for it is a pleasant process and the subject comes to it with more confidence. Eventually the preliminaries can be done away with. If the subject has a feeling of awe as he might have for a leader, healer or mystic priest or for one long heralded and much trumpeted, that will be an adjunct to his hypnosis, because he will obey more readily the command to concentrate on one sense; Mesmer wore lilac robes.

THE INDUCTION OF HYPNOSIS

The visual is the usual sense seized. Wells' method[2] in obtaining what he calls "waking hypnosis" may be taken as typical:—

> After a few preliminary experiments, he usually asks the patient to fix his attention on a simple object—a ring, a fountain pen, a point of light—and repeats to the patient some variation of the following:—
>
> "You must exclude all other thoughts and keep your gaze riveted on this point, eyeballs turned up as though you were looking at the middle of your forehead. Watch it steadily, fixedly, thinking of nothing else. Note every detail so that if I ask you to close your eyes you will be able to picture it as though you were still looking at it. You will be able to do this only if you give it your complete attention and literally feel that you are memorizing it. Watch it closely, try not to blink. Don't let your gaze shift to right or left . . .".
>
> When the patient seems to have succeeded in fixing his attention completely on the stimulus and has watched it steadily for several minutes, he is told:—

[1] "The Mechanism of Sleep" *The Practitioner*, March 1950, **164**, 261.

[2] *Journal of Abnormal and Social Psychology*, 1924, **18**, 389.

"Now close your eyes voluntarily as tight as you possibly can. Tight until they tremble. Tight until they tremble. It's all right if you have to make a face in order to do so. Just as tight as you can, eyeballs turned up, remember, just as if you were still looking at my fountain pen. Now I am going to count to seven and when I reach seven you will find that your eyes are stuck tight, and that the harder you try to open them, the tighter they stick. Your every effort to open them will have the opposite effect. They will be stuck tight just as if they were glued. One . . . two—tighter—three . . . four . . . five—tighter—six . . . seven. Now try to open them and you will find that the harder you try, the tighter they stick".

At the close of the session the subject is brought out of his trance by some such sentence: "When I say the letters A to H you will gradually come back to your normal self. At A your feet will move, at C your arms . . .".

Before dealing with the visual it should have been mentioned that a sense that is just below the facade sense and has no name may be monopolized for obtaining a trance-like state. Readers of "Kim" will remember how he threw himself into a sort of trance by repeating his own name. Many Asiatics have this power, and from the autobiography of Mahatma Gandhi one gathers that something of this sort accompanied his fasts; C. E. Montague and Tennyson have recorded similar personal experiences.

The auditory sense is sometimes seized for hypnosis; the subject lies with his eyes shut, the hypnotist's voice or music or some repetitive sound is made to dominate his consciousness: "Empty your mind of everything, but listen, listen, listen . . .".

I have never heard of *the labyrinthine*, *gustatory* or *olfactory senses* being seized as departure platforms for deliberate hypnosis, although, of course, they are commonly used as aids for obtaining sleep or in self-hypnosis—the swaying hammock, the half-sucked sweet, the Eau de Cologne on the pillow.

Muscular and joint senses are often seized to obtain hypnosis. This extract is taken from Bremman and Gill's "Hypnotherapy":—

"Before the hypnosis is attempted a number of manœuvres are often carried out, to serve as an introduction. The Kohnstamm phenomenon is a good beginning. The patient is asked to stand sideways against a wall and to press the back of his flexed wrist against it as firmly as possible, while keeping his eyes closed. This is continued for about one minute, the therapist exhorting the patient all the while to 'press with all your might, press with your shoulder muscles, your upper arm muscles, press till you tremble from the strain'. When the time is up the patient is asked to step away from the wall and stand with arms relaxed and hanging at his sides. In the majority of people, the arm in question will rise spontaneously in the air, often even to a 90° angle. The surprised patient is told that this feeling of relaxation and spontaneous movement of a limb is the kind of relaxation and feeling of surrender to external forces that he should attempt to adopt in the hypnotic induction".

But, of course, it is an induction, a trial induction.

The interlocking of the fingers, pressing them together for some minutes of concentration, and then being told that they cannot be unclasped is a common stage trick for selecting the more suggestible members of the audience.

The thermal sense is such a patchy and minatory affair in man that it is

not used for deliberate hypnosis; the hot bath for the maniac and the cold nose for the sanatorium patient are unwittingly used to induce sleep. In Pavlov's poor dogs, however, the seizing of the thermal sense and its tiring was rapidly followed by sleep:—

"Thermal stimuli are particularly apt to have this effect (of generalized or spontaneous inhibition) and if either warmth (45° C.) or cold (0° C.) be applied to the same spot of skin, repeatedly or continuously, the liveliest animals sooner or later become somnolent and may fall asleep".—Winton and Bayliss, "Human Physiology", p. 481.

The tactile sense has often been used for hypnotism. Valentine Greatrakes (1628), and many before and after him, obtained his cures by stroking with his hands, and Robert Boyle went to witness them.

NATURAL INDUCTION

To correlate the magic process of hypnotic induction with the trite and trivial of everyday life: the man in the armchair, gazing into the fire before his eyes close is unconsciously seizing the visual platform for the regressive passage of sleep; the man asleep in the railway carriage seized the auditory or the labyrinthine; the pulling of moustaches, stroking of hair, patting of feet in moments of stress are the reverse process, attempts to keep other senses alert and alive.

To illustrate that sleep comes irresistibly if the senses are truly reduced to one line, perhaps I may be permitted to trot out my own guinea-pig:

As a result of meningitis in childhood I have the use of only one ear and therefore also lack that third sense, a sense of direction. I have even mistaken borborygmi, my own or another's, for someone at the door. If, being moderately sleepy and with eyes shut, I listen to the wireless I am asleep in a few minutes. If the subject is one that interests me or is likely to interest me, paradoxically I am asleep much more quickly than if I am indifferent to it. Time and again I have thus missed what I wanted to hear.

When I was a student I used to go with others to a country holiday home for London boys. We used to take turns in telling them stories when they were in bed at night. The greatest artist in story-telling among us could have them all asleep in ten minutes—his technique was by a thrilling opening to get their attention, then invoking placid imagery, by repetitive phrase and monotone, and a yawn or two and they were all off, and he could tiptoe out of the dormitory. The significance of the arresting opening dawned on me thirty years afterwards.

THE HYPNOTIC STATE

Hypnotic sleep is indistinguishable from ordinary sleep; there is only one sleep process—which we have already outlined. Differences in sleep are in levels of the sleep process, in the speeds of the process, and the patternings it leaves behind.

But sleep is not an essential part of hypnotism. A person in the hypnotic state is as putty in the hands of the hypnotist; he may be sent to sleep or

not. When he is being hypnotized, when he is being reduced to one sense, he must lose all critical power. He cannot say, for instance, this man's fingers stink of tobacco juice or he has a slight squint. He therefore becomes boundlessly suggestible. If he is told he is a king or a clergyman or a musician he will straightway behave as he conceives a king or clergyman or musician should behave, his voice will alter with his identity; if told to see a picture on a blank wall he will do so and describe it in detail; if told there is no one in the room he will not see a crowd, he will be tireless in some heavy manual task, stay statued in some ungainly pose, nor feel the needle thrust into his arm, and—if he is a patient, not an experimental subject—he will forget the shamming muscles that would hide from alien eyes some lack elsewhere, or go once more to that inferno where the battle robbed his wits, be puppet and automaton of him, who wills, and then—forget it all. Forget everything as a dream is forgotten, yet remember some message from the master mind, some vital message as the servant thinks, some act to time, some detailed ordinance.

The whole thing is fantastic. That has always been the first response to hypnotism. As the child said about the giraffe and the mandrill, they are too absurd to be real; it is play-acting; it is fraudulent; in any case it has nothing to do with serious science. "Some three centuries of enthusiastic investigation and of bitter controversy were required to establish the occurrence of the hypnotic state among the facts accepted by the world of European science" says the *Encyclopædia Britannica*, and any intelligent person seeing hypnotism for the first time recapitulates these centuries in his mind. To us, looking at it from the naturalist's and functional point of view it may seem amazing that an individual whose every device has been for self-preservation should throw away his native wit, the defences that he learnt in youth, his manhood's watch and ward, and become as putty in the hands of a stranger. But then man is not an individual, he is a gregarious animal, an animal who through countless centuries has developed as a member of a group, and, as Bertrand Russell pointed out in his Reith lectures, of a small group, the enlarged family, the clan, the tribe, and—thousands of years later—of the village. To the naturalist's nostrils this hypnotism stinks of some corporate function, some atavism of the spirit of society, some sacrificing of self for survival. Let us look at it from that point of view.

PRELUDE TO PARLIAMENT

But first of all we must try to remove a few natural human reluctances in ourselves. When one looks back in history the hills seem clustered together and the foreground a long life's march. The Roman occupation of this island seems like a week-end, whereas it was as long as from Elizabeth to now, and of the time before the Romans we think of while we yawn. As in dreamless sleep, unrecorded time is passed in a flash. Yet, in the many,

many thousand years, when the genes that gave rise to us were scattered over Europe, was modern man formed, and in essentials unalterably formed. After this period, when man must have been standardized by privation, he blossomed out, and "The Golden Bough" tells us with what wonderful diversity. Recorded history is but man's success story as a species.

Another human reluctance, seen in every generation, is a blindness to the implications of the known fact that we are part of a continuum. Professor Tanzi says in a chapter on paranoia that no intelligent man reading for the first time the Christian story and doctrine would regard it as anything more than an interesting anthropological record. This would be true of all the world religions, but we of the Christian tradition may at any rate exercise the truly Christian virtue of humility and not deny our poor savage mothers who trudging in countless succession looked over their shoulders to their long foregrounds in our deceptive hills. Not that it matters much, if we do deny them—their sons will bob up all right.

I was once in a group of adult men, when the Prince of Wales came among them. The change was remarkable: they became excited in a subdued way, more corporate, more belligerent, self-displaying, yet self-sacrificing, centralized on him, almost anæsthetic to other matters or—let me put it more clearly—other matters had no emotional content, so did not interest them, uncritical and extravagant in expression, "Magnificent chap", "Terrific sportsman"; there was a refreshing regression to boyishness among them. Some were so-called "hard-bitten" business men, some were scholars. None escaped the infection; certainly not I.

I have seen (and felt) this emotional release and centralizing on a person even at a B.M.A. meeting. It can be observed in politics; it accounts very largely for the wonderful effects of speeches—like Gladstone's—which are so vapid in print. In the individual its essence is that criticism is numbed, and if you analyse that you will find that it originates from a numbing of all the senses except one, which is most often the visual, but auditory in the case of the speeches; it is accompanied by an emotional flooding, a burgeoning of the spirit. That is in the individual. In the body corporate it is contagious, unifying and raises hostility to and in other groups. Those who are integrated enough to feel back to their prepuberty days will recall it in a dominating form as the "gang spirit". It is intensely unifying in small numbers and exclusive. For reasons to be explained it is more intense in the male. In the modern world it can be seen in the personnel of orders of chivalry, of clubs, and of suburban railway carriages. No, our mothers and fathers of the steppes are not far distant. Let us slip off our finery and see them in the flesh.

PAUSE AFTER PRELUDE

There is just one other human reluctance to be removed. It is significant of the limitations of the human mind that extremes beyond its daily ambit in quantity and quality after a momentary excitation repel rather than attract:

astronomical affairs may for a moment or two amaze, but they are not allowed to intrude into our daily thought, our philosophies, our religions; the biography of A. Jones by B. Jones, which depicts a life of unparalleled splendour fails to grip us; cosmic forces and countries and ages must be personified to make them intelligible to our myopia. We prefer the biography of, say, Dr. Crippen, who was human in some imperfections; we like to see our God in little kindnesses.

But here, to understand hypnotism, we have got to get into our minds this wide fact: that recorded human history is negligible in time compared with the unrecorded, that there were many, many millennia of moulding by weather, food and foe, and all the while it was not the individual, it was the group that was being faceted by time and tribulation, it was the group that must survive; damn the individual and the devil will dam his genes; it is essential to realize this because, as Æneas modestly puts it, *quorum pars magna fui*, when he really meant, "I was—and am It". We must realize the formative millennia of man, not as a judge reads a prisoner's record, but as the prisoner knows it.

THE PROTOTYPE OF PARLIAMENTS

The tribe that acted as one under a leader would have enormous advantages in warfare, in hunting and in privation. The advantages to the leader and led would be inherited; the rabble would leave none to inherit.

It is not hard to imagine a scene which in its essentials must have been repeated millions of times in our unrecorded history: the wind shrieking over the steppes, the fire in a sheltered hollow, the clustered tribe, the debate, limited to about thirty words, gestures and the scale of emotional tones; the subjects—food, most often, for a ravening belly gives no rest; sometimes them, them, them, the enemy, the grievance growing as they growl, some bison which we wounded and they found and ate; sometimes, seasonally, she, she, she, woman, which gives the Freudians their for-ever-April ideas.

Freud, in "Group Psychology and the Analysis of the Ego", compares hypnotism to being in love. He says: "There is the same humble subjection, the same compliance, the same absence of criticism toward the hypnotist just as toward the loved object". He does, however, trace the "uncanny" and coercive characteristics of the phenomena of group psychology and hypnosis to their origin from the primal horde, conceiving of the relation between subject and hypnotist as well as that between group and leader as a reactivation of that of the individual member of the primal horde to the primal father.

Then the emergence of a leader, not necessarily the best hunter or the best fighter, but the best practical mind, the best planner, the best talker and gesticulator, the most popular. What more desirable qualities could a leader ask for in his followers than those which we think of as characteristic of hypnotized persons: suggestibility, obedience, tirelessness, indifference to pain, forgetfulness of the incident when it is over, yet with an implacable memory for orders to be carried out after battle? Are not these characteristics

summed up in one adjective which we applied to the armies of the Mahdi, of Hitler, and of Japan—fanatical? Is not this the very acme of function, function in a race-surviving form? Although these armies were beaten they would never have come into being without fanaticism, and history bristles with its triumphs.

Then imagine ourselves on the outskirts of this prototype parliament: dusk after dusk it goes on, only coming to crisis or orgasm once in a few moons, listening to our leader, identifying ourselves with him, imitating his every gesture (as those in latah in Malaya and the French-Canadian "jumpers" do), sharing his hatreds, his humour, his hunting lusts, our adored leader, our God's right-hand man. "The deliberate induction of states identical with or closely allied to hypnotism is practised by many barbarous and savage peoples, generally for ceremonial purposes", says the *Encyclopædia Britannica;* our comment is that ceremony and ritual in origin are practice, like play at the nets.

As and when the session comes to crisis or orgasm we get on the same colour in the emotional spectrum as our leader, so criticism is impossible for those who feel it, as in our Parliament when Neville Chamberlain came back from Munich; the whole function of hypnotism is unity for survival, as in America after Pearl Harbour; all normal people can be hypnotized, the sort of person the stage hypnotist uses is the sort of youngster who would join up on the first day of war; it is a pleasant process and part of the pleasantness is the feeling of individual surrender; man has never been so individualistic as now, but he reverts very quickly on crisis and long before that the whispering early stages of suggestibility can be heard in Throgmorton Street; the forgetting of the trance is seen in the real warrior's silence about his experiences.

THE FEMALE'S PART

So far we have dealt only with the males of the species. The female is a less differentiated being; every human characteristic is hers; she feels these tribal urges but not to the same degree, she is less obsessed by them and in public matters and ceremonial has a comparative lethargy; she enjoys that lack of constant stimulus always seen in the "haves"; she has forty-eight chromosomes.

The male, on the other hand, has only forty-seven and a bit; *qua* male the only known gifts he can transmit to posterity are one form of webbed toes and a revolting skin disease; so far as propagation is concerned one male to twenty females would be ample; he has the constant stimulus of his inferiority to keep him restless, with the result that muscularly, mentally and socially he is woman's superior after puberty—before puberty women show the superiority of the comfortable two per cents, plus bonus; the male is the poor boy who makes good in a thousand ways; his is the sex on which natural selection chiefly acts; defence with its imperative necessity for acting

in unison has fallen to his lot, ceremonial and ritual which were and sometimes are practice for defence are also his; he can be sacrificed in large numbers without serious threat to the species; unless diseased and except temporarily he can never be satisfied because of that crippled Y-chromosome; as the poet might have written:—

"The little more, how much it is;
The little less and hell's to pay".

These differences, thank God, are not cumulative, because every female carries half her father's genes.

PRELUDE TO CORRELATION

The essential need for unity in the primitive group which resulted in a leader with the most cunning brain and followers with characteristics which we now regard as those of hypnosis is such a fundamental defence mechanism in man that he reverts to it in times of stress, whilst in times of peace and prosperity it has grown to become the framework of his social structure. This is not the place—nor the author—for a survey of this growth, but a few random observations may indicate how vital is the primitive group system now in our midst.

Groups have taken on a thousand aims—trade, moral, diversional, scholastic, recreational. The best talker generally becomes leader, but from the earliest times in history there has been a tendency for the idol or emblem to supplant the leader. A dead leader is a good compromise; founders are idols on a pedestal of authenticity. Groups still raise hostility to those not in the group; Masons, all old-school-tie groups, as well as that fearful gang of hooligans in the next street, all flourish in a medium of hostility. The suggestibility of those in the group is seen in their taboos, things that are not done; the negative hallucination can be demonstrated in a really keen member who will not see anyone not belonging to his group; the anæsthesia which is such a real thing in hypnosis that Esdaile was able to do three hundred major operations under it, and in battle that wounded soldiers often do not know they have been wounded, can be seen in a willingness to undertake long and onerous tasks as well as the most painful athletics.

Women do not enter into the group spirit with the same intensity; their minds are always hovering between the view that their menfolk are small boys playing secret societies and Red Indians and that here are sacred mysteries which they themselves are unworthy to enter.

But—but the greatest nobilities of humanity, its best self-sacrifices, self-effacements and loyalties to the end have been under some modification of the tribe or group system. The spirituality of the group aims is cheapened or destroyed by being verbalized, but sometimes the poet with his condensations and meanings in depth can convey something of their glory to the

acolyte. Newbolt, addressing a boy somewhere about the turn of the century, wrote:—

> "God send you fortune: yet be sure,
> Among the lights that gleam and pass,
> You'll live to follow none more pure
> Than that which glows on yonder brass.
> 'Qui procul hinc', the legend's writ—
> The frontier-grave is far away—
> 'Qui ante diem periit:
> Sed . . .' ".

But even the Latin begins to sound like hobnail boots round altar rails. It would be the merest parochialism, the blindness of the group itself, not to realize that the same aura of sanctity, the same gleaming light, comes from the swastika to the young Nazi, from the hammer and sickle to the young Russian, from the star of Israel to the young Jew. Their calls must always be stronger when the storms come because they are founded not on recent reasoning, but on the schooling of the steppes and desert places.

Hypnotism then has this historical background and may be regarded as the subjective side of a group defence mechanism, which in modern life has been greatly elaborated. That rather despicable exhibition—stage hypnotism —flourishes because it shows hypnotism in a crude and primitive form and excites amazement and wonder; it is like stealing temple fire for Catherine-wheels.

CORRELATION AND SUMMARY

Hypnotic or natural, alcoholic or drugged, there is only one road to sleep, and our caravans lumber over the ancient route, whitened by the bones of animals long before the time of man. The stages are fixed, but sometimes we travel over them quickly, sometimes we are halted by shadowy Bedouins or dally at a caravansarai; rarely we may not reach the Mecca of our making because the dawn beckons back again; this probably gives as good an idea of the physiological process of sleep as talk in terms of "dissociation".

As in the action of alcohol, the sleep process starts when all the faculties, emotions and senses are in full play, contradicting and confirming, cross-bearing and criticizing, and one drops out, then another, then another and then in settled sequence. It is a graduated process and there is no one point where it can be said, "Here, he goes into sleep". Many adults habitually wake to the extent of bringing dreams to match their worries half a dozen times a night, but even in their tossing they are some way in regression. Gillespie has pointed out what very little effect years of insomnia have on the sufferer, and it seems probable that in each person there is a sort of regression-expression balance; put in the vernacular, if one is as "bright as blazes" for X hours one must be "dead to the world" for X hours or half-doped all the time or any intermediate equalizing of vitality. Normally on waking, generally with distaste, we see ourselves doing what we have got to

do too soon: the cold bath, catching the 8.15, being matey with Carruthers, what one might call the anticipatory level, which has obvious preparatory functions. That would seem to be the dividing level with ordinary life on one side and sleep and hypnosis on the other.

The hypnotic state is a social function of the upper part of the sleep mechanism. Normally it can be brought into play by a community need; artificially it can be induced in all except the psychotics.

Somnambulism is a hypnotic state caused by an endogenous compulsion. The only one I have had the luck to study had the compulsion from a fairy story, in which, presumably, she had identified herself with the poor princess, who had to go looking for some talisman.

There is nothing unusual in the fact that the sleep mechanism is used also for the social function of hypnotism. It is the rule rather than the exception for one mechanism to have more than one function, e.g. respiration also serves as motive power for talking, singing and oratory; in birds, feathers supply locomotion, warmth, and sexual hoardings; in dogs the urinary excretion is also used for leaving mystic messages; sleep itself is used for solving difficulties.

Nature, that trial-and-error Dame who shaped us, has squeezed every ounce of function out of our limited workings, and she has had unlimited time. Peoples or groups under the influence of social hypnosis are without insight into their own condition. Other peoples and groups watching them are filled with feelings of the infra-red end of the emotional spectrum, fear-hostility-superiority: "the old-school-tiers", "the mad English", "the fanatical Japanese", "the Hollywood fans".

Given the proper threat to existence or survival all peoples and groups will react almost instantaneously in this way, not even excepting readers of *The Practitioner*.

> "Sweeps the wind to-day o'er the steppes the same as ever?
> Cluster darkling figures by the fire?
> Sounds the voice they echo, echoing never to fade nor tire?"

Well, with reservations and modifications, yes, yes, oh yes, I think so.

CURRENT THERAPEUTICS

XXIX.—THE ANTIHISTAMINE DRUGS

By C. J. C. BRITTON, M.D., D.P.H.

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HISTAMINE is closely related to the amino-acid histidine and, in fact, is histidine with a carboxyl group removed. It was discovered by Windaus and Vogt in 1907, and Dale and Laidlaw in 1910 demonstrated that it plays a most important part in the production of anaphylaxis in animals. They showed that injections of histamine cause contraction of smooth muscle, dilatation and increased permeability of capillaries, a fall in blood pressure, and increased secretion of various glands. These are the effects found in man in allergic diseases such as asthma, hay fever and urticaria, and so it was considered on this and other evidence that histamine was the most important chemical initiator of the allergic reaction. It has been stated as a practical theory, although the evidence is by no means conclusive, that in an allergic reaction the antigen, e.g. pollen, when taken into an allergic person unites with preformed antibody substances in the cells, causing damage to the cells and liberation of histamine, which then leads to the allergic reaction. In immunity it is postulated that the union of the antibody and antigen takes place in the blood or tissue fluid and so no histamine is liberated.

The results of the discovery of histamine led to a search for substances which would neutralize its action. One reasonable approach seemed to be to attempt to desensitize patients against histamine by a series of injections of ascending dosage of the compound itself, but histamine is not antigenic and no good results were obtained. More recently histamine azoprotein, in which the histamine is united to protein and thus acts antigenically, has been used but the results have been disappointing. Injections of histaminase, a natural enzyme which destroys histamine, have also been used but these are quite ineffective *in vivo*.

It was not until 1937 that the French workers, Staub and Bovet, reported the anti-anaphylactic effect in sensitized guinea-pigs of thymoxy-ethyl-diethylamine. This substance was, however, too toxic for clinical use. Research proceeded apace and the first effective clinical compound was reported by Halpern in 1942 and called 2339 R.P. ("antergan"). This was followed by the discovery of 2786 R.P. ("neoantergan", "anthisan"), a closely related compound, by Bovet *et al.* (1944); of "pyribenzamine" (Mayer *et al.*, 1945), and "benadryl" (Loew *et al.*, 1945) in America. Since then scores of allied compounds with antihistaminic action have been produced and many put on the market, while the search is still furiously proceeding for drugs of greater potency and less toxicity.

MODE OF ACTION OF THE ANTIHISTAMINE DRUGS

Such drugs may prevent the pharmacological action of histamine in three ways:—

(1) They may prevent the release of histamine from the tissues. This is largely excluded by the fact that antihistamine drugs do not prevent gastric secretion by histamine, a known physiological action of the substance.

(2) They may neutralize the histamine by direct combination with it. Work by Staub (1939) seems to exclude this possibility.

(3) They may increase the action of adrenaline, which then counteracts the histamine effects. This has been disproved by the fact that a number of the more recent antihistamine drugs actually antagonize adrenaline.

This leaves us with the theory that the antihistamines block the action of histamine by competing for its tissue receptors in the so-called "shock" tissues. This would bring the action of the drugs in line with the mode of action of the sulphonamides in blocking the receptors of the essential metabolite of bacteria, para-aminobenzoic acid.

DOSAGE AND ADMINISTRATION

Table 1 gives a list of the preparations at present available in this country and the form of administration.

Before discussing the actual diseases and the use of these drugs, it must be stated clearly that the efficacy of these antihistamines in the clinical case does not necessarily parallel their order of potency as found in animal experimentation with anaphylactic shock or in isolated smooth muscle preparations. One important reason for this is the presence of certain effects which they cause other than their antihistamine action. Thus they have a varying degree of anti-acetylcholine effect; they also have a quinidine-like effect, a local anæsthetic effect, and may cause drowsiness and other side-effects. These side-effects may be beneficial in certain cases and detrimental in others. But even more important than these side-effects is the individual reaction of the patient, who may react well to one compound but may not tolerate another of equal experimental histamine potency.

Antihistamine drugs are almost always given by mouth in tablets, capsules or, for small children, in elixirs. Ampoules for injection are also put up for anthisan, benadryl and phenergan but have no real advantages over oral preparations, which are rapidly absorbed. If an extremely rapid effect is required, adrenaline is still the drug of choice. Parenteral injections are not without danger.

Dosage.—The usual dosage of phenergan and thephorin is 25 mg., with a maximum dose of 150 to 200 mg. in the twenty-four hours; of benadryl, histantin and pyribenzamine, 50 mg., with a maximum dosage of 400 mg. in the twenty-four hours; of antistin and anthisan, 100 mg., with a maximum of 800 mg. in the twenty-four hours. These are usual adult dosages but may

be increased somewhat if unpleasant side-effects are absent and if a pharmacological effect is not present. Children tolerate the antihistamine drugs very well, and adult doses may be given to children over the age of twelve, with the limitations mentioned below. In smaller children the elixir preparations are more valuable and the best technique is to begin with 1 teaspoonful (4 ml.) of the elixir available (anthisan, benadryl or pyribenzamine) and increase within the dosage already mentioned until a clinical effect is reached or side-reactions preclude further administration.

TABLE 1

Proprietary Name	Manufacturer	Non-proprietary Name	How Available	Dose or Concentration
Anthisan	May and Baker	Mepyraminemaleate	Tablets Tablets Elixir Ampoules for injection Cream	50 mg. 100 mg. 25 mg. in 4 ml. (1 teaspoonful) 25 mg. per ml. 2 per cent.
Antistin	Ciba	Phenazoline	Tablets Nose and eye solution (with privine 1:4000) Cream and ointment	100 mg. 1:200 2 per cent.
Benadryl	Parke Davis	Diphenhydramine	Capsules Capsules Elixir Cream Ampoules for injection	25 mg. 50 mg. 10 mg. in 4 ml. (1 tablespoonful) 2 per cent. 10 mg. per ml.
Histantin	Burroughs Wellcome & Co.	Chlorocyclizine hydrochloride	Tablets	50 mg.
Phenergan	May and Baker	Promethazine hydrochloride	Tablets Tablets Ampoules for injection	10 mg. 25 mg. 25 mg. per ml.
Pyribenzamine	Ciba	Tripelennamine hydrochloride	Tablets Elixir	50 mg. 20 mg. in 4 ml. (1 teaspoonful)
Thephorin	Roche	Phenindamine	Tablets Ointment	25 mg. 5 per cent.

The effect of a single dose does not last for more than six hours, and usually much less, although the action of phenergan is said to be more prolonged, so that in order to maintain a proper concentration when a continued effect is required, as in urticaria, the drug should be given three or four times a day. As many of these drugs (an exception is benadryl) may

cause increased motility in the alimentary tract and nausea on an empty stomach, they are best given after meals or with a well-sweetened drink. Tolerance to the antihistamines does not appear to occur.

SIDE-REACTIONS

These differ markedly in their incidence from case to case; more so than from drug to drug in comparable dosage. Certain drugs, like benadryl, cause a much greater proportion of side-reactions, especially drowsiness, than others like histantin, but the drowsiness induced by benadryl and others may be a clinical side-effect of considerable value, as in urticaria at night and nocturnal asthma in children. The percentage of side-reactions, as recorded in one report covering 200 to 300 cases, may be 60 per cent., and in another using the same drug 30 per cent., so that the individual reaction to the drug is more important than the fact that such side-reactions may occur. One patient may sleep for many hours after a single tablet or capsule, whereas another may have no drowsiness after 4 tablets or capsules.

It is impossible in the space of this short article to detail the side-reactions found with each of the drugs available and their relative frequency; further guidance in choice of drugs will be given later. The following list, whilst not exhaustive, covers the usual side-reactions and their order of frequency from above down. As has been mentioned, drowsiness is more common with drugs like benadryl, whilst nausea and diarrhœa are more common with anthisan.

Drowsiness
Dizziness
Weakness
Nervousness and mental incoordination
Nausea
Headache
Diarrhœa
Tinnitus
Vomiting
Irritability
Dryness of the mouth
Tachycardia

The drowsiness and feeling of weakness can often be minimized by giving 5 mg. of amphetamine or of coramine-caffeine coincidentally with the daytime doses. It is often found that the patient rapidly becomes tolerant to the hypnotic effect if the drug is continued, so that if the anti-allergic effect is good, the drug should be continued to see if such side-reactions will disappear. The possibility of side-reactions must always be realized completely by the doctor in prescribing these drugs, and the patient be warned. The first dose of any of the drugs and any increase in dosage must be given at a time when the patient will not be called upon to perform skilled

movements depending upon acts of judgment, e.g., driving a motor car.

Recently, Cherry (1949) has reported a labyrinthitis developing in three cases on withdrawal of antihistamine therapy. Again, several children have died through taking the brightly coloured and sugar-coated tablets when left within their reach. The possibility of these happenings leads to the hope that the antihistamine drugs will soon be included in the Poisons Schedules.

TREATMENT OF INDIVIDUAL ALLERGIC CONDITIONS

I would again stress at this point the importance of the individual factor in the clinical use of the antihistamine drugs. One patient will react well to one drug and not at all to another which on animal experimentation should be more potent; again, he may show severe side-reactions to one drug and not to another even in twice or four times the dose. In our present state of knowledge the best method in clinical practice is to try one after another of the drugs available to find which drug suits the patient best. When drowsiness is required as a side-reaction, benadryl is probably the best to use first. In view of this soporific effect it is well not to use these drugs in combination with barbiturate until the tolerance of the patient is discovered. Again, since many of them have an atropine-like action, this latter drug should also be avoided until the effect of the antihistamine alone has been noted. Antihistamine treatment, if a big dosage is given, should never be terminated suddenly, as this may precipitate a recrudescence of lesions more violent than before treatment (Hunter and Dunlop, 1948). The dosage should be tailed off gradually over several days.

Urticaria and angioneurotic œdema.—These conditions in their acute form are the ones which react best and most regularly to the antihistamine drugs; it does not appear to matter whether the condition is due to food sensitivity, to predominantly psychological causes or to drug sensitivity, there is almost always one or more of these drugs which, when given in adequate dosage, will provide excellent relief. At the beginning the drug will probably need to be given three or four times a day, whilst as the attacks lessen it can be given night and morning, then at night only, and finally only if symptoms recur. It must be remembered that in emergencies such as swelling of the tongue or œdema of the glottis, treatment with adrenaline is necessary, and the antihistamines should be given to prevent recurrence.

Hay fever.—Antihistamine drugs improve or relieve the symptoms in some 70 per cent. of cases. The dosage required depends upon the individual and often needs to be high. The drugs should be given at the onset of symptoms at any time; a dose late at night will often prevent the early morning recrudescence. There is one disadvantage to the regular use of these drugs from year to year without any specific hyposensitization, and that is that the incidence of asthma appears to be increased. This has been my own experience and has been stressed in a recent report of the American Academy of Allergy.

Asthma.—The use of antihistamine drugs in this condition has been very disappointing, at least in adults. Occasional cases are benefited and most of the benefit is obtained in the prevention or relief of night attacks (Herxheimer, 1949). When the drug is effective it is its sedative effect that is probably of most importance. In severe attacks the antihistamines are of little value. In younger children, however, the antihistamine drugs are usually of considerable value in the prevention and relief of asthmatic attacks. I usually recommend that if the child has a cold, is over-excited or over-tired, one to four teaspoonsful, or even more, of one of the elixirs should be given prophylactically before going to bed, and the dosage repeated in the night if the child awakes coughing or wheezing.

Vasomotor rhinitis.—Some 50 per cent. of cases have symptomatic relief from the use of these drugs. A prophylactic dose before going to an important meeting or party is often of great value, and a dose at bedtime may keep the patient clear throughout the night. Again, as in hay fever, investigation of the cause, and desensitization when possible, should not be neglected.

Allergic eczema.—Antihistamines may be used in two ways in this condition or group of conditions. To relieve the irritation the drugs may be given in the usual dosage, three or four times a day, the last dose at night being greater than the daily doses, since it is when the patient is warm in bed that the irritation is usually most severe. The drugs may also be applied locally in a cream to relieve the local irritation. They have a powerful local anæsthetic effect in most cases, and thus by reducing the scratching they help the natural healing forces. It is important, as with the trial of any ointment or cream in a dermatitis, that the patient be warned to try the effect at first on one localized area of skin, and only if no irritation occurs should a general application to all the affected areas be made.

Miscellaneous conditions.—Drug sensitivities have been mentioned before and the value of antihistamines described. *Bee* and *wasp stings* are often relieved, as regards general reactions, by antihistamines when adrenaline is not available, or as an adjunct to adrenaline, whilst local application of antihistamine cream modifies the local symptoms. *Travel sickness* has been helped by these drugs, particularly by "dramamine" (Searle and Co.), which is not yet available in this country. However, from personal experience of the latter drug, despite reports in the literature of the complete absence of side-reactions in trials made, I can state that these side-reactions may be worse than the seasickness.

THE COMMON COLD

Finally, reference must be made to antihistamine therapy in the common cold. This problem is made difficult by the facts that many so-called "colds" are allergic reactions and are not due to virus infections; that the natural course of the common cold is so variable, and that control of the

enthusiastic patient is so difficult. In my experience these drugs do appear in some cases to lessen the rhinorrhœa in the early phases and make this stage more comfortable. However, the dangers of the indiscriminate use of these potent drugs, with all the possible unpleasant side-reactions, far outweigh the possible benefits. In an important report of the Council on Pharmacy and Chemistry of the American Medical Association (1950) the literature on the subject to date is reviewed. It is concluded from the papers that there was no certain scientific evidence that the patients treated necessarily had colds and in over half of the cases investigated there were either no controls or inadequate controls. The antihistamine drugs certainly could often produce subjective relief owing to inhibition of the nasal discharge, but similar results may be obtained by atropine and ephedrine and there was no real evidence of cure. Finally, although severe toxic reactions to the drugs are rare, serious affections of the central nervous system, the genito-urinary system and the hæmopoietic system have been recorded. The trials of antihistamine drugs in the common cold by the Medical Research Council are awaited with great interest.

SUMMARY

The antihistamine drugs are an important addition to our symptomatic therapy of allergic disease. The best drug to use depends more upon the individual than upon its antihistaminic potency as shown by animal experiments. The drugs are dangerous, and initial doses should be low and given at a time when the patient is not called upon to do skilled movements depending upon acts of judgment. The antihistamine drugs are not a cure, and a search for and, if possible, eradication of the causes still occupy the most important place in the treatment of these conditions. When sensitivity to extrinsic allergens can be found and proved by testing, desensitization offers an excellent chance of relief.

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REVISION CORNER

THE TREATMENT OF PRURITUS ANI

ITCHING of the anal region may be associated with a multiplicity of causes, both general and local, and the treatment calls for the discovery and elimination of these causes, if possible.

CAUSAL FACTORS

Local causes include parasites such as *threadworms* (the most common cause of itching in the anal region in children): attention to prevention of auto-inoculation and treatment by "diphenan" or quassia are lines of attack. Parasites externally may produce itching at an age when there is hair growth in the area, namely *phthiariasis pubis infestation*, calling for DDT or other antiparasitic therapy.

Infections by *fungi*, *yeasts* or by *pyococci* may cause an irritable dermatitis of the area. These infections are amenable to treatment in their earlier stages, before secondary thickening or undue sensitivity with obvious eczema reaction develops: Castellani's fuchsin paint or 1 per cent. aqueous solution of gentian violet in the case of fungus or yeast infections, and topical penicillin, "vioform" or other antiseptic preparations in the pyococcal cases.

Allergies to *substances ingested* or *inhaled* (foods, pollens) are stated to produce eczema of the anal and vulvar regions in a number of cases; in fact Hailey (1949) stresses heredity and the presence of eczema elsewhere in many cases.

A combination of local causes may produce *pruritus*, for example stasis (in pregnancy, pelvic tumours), hæmorrhoids, hypertrophied tags, fissures, fistulæ, verrucæ acuminatæ, chronic constipation (effects of pressure and the passage of hard scybalous masses), polypi, one or more of which, associated with lack of cleanliness, sweating, leak of mucus, and the like, may lead to pruritus. *Contact irritants* may also produce an eczematous reaction and itching: for example, liquid paraffin oozing through the sphincter, toilet paper (especially medicated), toilet powder, sanitary towelling, toilet seat chemicals (such as lysol), clothing (wool, silk, fabric finishes), nail varnish, soaps, medicaments (particularly cocaine and morphine). Pressure of tight clothing may induce pruritus, which is experienced immediately after its removal.

Lesions of various dermatoses which may affect this region may be pruritic, e.g. psoriasis, lichen planus. General diseases may be accompanied by pruritus ani, e.g. hepatic or renal diseases, prostatitis, cystitis, appendicitis, carcinoma, diabetes (in this latter the cause is probably a local effect of the urine, with its encouragement of monilial infection extending to involve the anal region).

Endocrine factors, particularly menopausal, may be of importance and, in my experience, such cases respond reasonably well to appropriate hormone treatment, but often require heavy dosage; for example, when an œstrogen is indicated, ethinyl œstradiol may need to be given in dosage of 0.025 mg. or even 0.05 mg. daily (unless bleeding is induced) for a spell, to control the symptoms: care must, of course, be taken to reduce the dosage very gradually. These cases are usually associated with pruritus vulvæ, although the severity in the two areas may vary inversely.

THE PSYCHOGENIC FACTOR

Sutton (1949) maintains that a local pruritus has usually a local cause, but others,

e.g. Sequeira, Ingram and Brain (1947), hold that many cases are associated with psychogenic factors, and Ormsby and Montgomery (1948) find that the histopathology in these cases is that of neurodermatitis, not that of a contact or infective dermatitis. In my own experience there is a large group of cases in which neuropsychiatric factors seem to predominate, even when there may be some local precipitating factor: many of these cases show lesions of neurodermatitis elsewhere, whilst others show no macroscopic objective skin changes. Of course the effects of oft-repeated crises of pruritus, with consequent loss of sleep, in themselves tell on patients, but do not explain, for instance, the onset of pruritus coinciding with a husband's capture by the Japanese during the war, or with marriage and, from ignorance or intent, the practice of coitus interruptus as a method of contraception, to mention only two of many examples, including a case of admitted homosexuality (repressed).

It is with this psychogenic group that I shall deal mainly, as I feel that they comprise the majority of chronic cases of true pruritus ani (sometimes associated with pruritus scroti or pruritus vulvæ), with its intense crises of itching. Of 42 cases I have seen at hospital in the past two years, 33 were of the neurodermatitic type, and of 87 seen among an analogous number of patients in private practice (over a much longer period of time, however), 43 were of this type. Among the 129 cases the vast majority (95 cases) were between thirty and sixty years of age and only one case (a boy of nineteen years) was under twenty years. But the general rules for this type (which are an essential accompaniment of any psychotherapy—and this must be in the hands of an expert in this class of patient, often of an obsessional type) can be applied with advantage to all cases.

TREATMENT

In the relief of pruritus I have found the *antihistamine drugs* a great help, but the dose may have to be full: "phenergan" may be given, when tolerated, in divided doses, to a total of 200 mg. in the twenty-four hours, although a small dose (25 mg.) two or three times during the day and a large dose (100 mg.) at night may be more effective. "Thephorin", in doses of 75 mg. to 150 mg., or even 200 mg., in the twenty-four hours is less often hypnotic or nauseating than phenergan, but in some cases has a stimulating effect, and this may necessitate substituting a sedative (e.g. phenobarbitone, ½ to 1 grain (32 to 65 mg.)), for the night dose. "Histantin" I have used in dosage of 100 mg. to 300 mg. in the twenty-four hours, with only slight drowsiness complained of in a few cases. Heavy dosage, however, must not be given initially to those called upon to drive any mechanically propelled vehicle, but a tolerance to quite a large dose can be worked up over the course of a few days by gradual increase from small doses.

Hygiene.—Catharsis should be avoided, as fluid stools irritate the anal skin, but it should be noted that thephorin particularly, among the antihistamines, may be constipating. I consider that reasonable doses of cascara or an analogous laxative may be employed if required, but liquid paraffin should be avoided. Toilet paper should not be used, the area being bathed with cotton-wool and warm or even cold water after defæcation: starch may be added to the water with advantage. The area should be bathed at least once or twice during the day in addition, from the point of view of cleanliness. Clothing should be loose and smooth, preferably

cotton or linen next the skin. Baths should be taken tepid, and in mild cases soap may be used once daily, but in other cases is best avoided.

Prevention of scratching.—As many patients can control their scratching when awake, but often waken during the night to find themselves scratching furiously and can do an immense amount of damage in the few moments before reaching full consciousness, some restraint of the hands is advisable, and a simple method, advised by Bettley (1949), is to put the hands in white cotton gloves and hang these round the neck by tapes which are long enough to allow of comfortable movement, but not long enough to let the hands reach the anal region or perineum.

Local applications of a non-greasy type are generally advised, such as calamine lotion, to which 1 per cent. phenol, or 0.1 to 0.5 per cent. camphor, has been added: a lotion can be applied as a compress on gauze at night and dabbed on during the day. Powder may be adequate, e.g. camphor 0.5 to 1 per cent. in talc, or a powder of bismuth subnitrate or subgallate, talc and French chalk. In a number of cases, however, an antihistamine drug applied in a cream may be exceedingly useful: anthisan and phenergan have been of benefit, in my experience, in a 2 per cent. concentration, or thephorin ointment, but intolerance may develop. At a later, lichenified stage 10 per cent. crude coal tar in acetone as a thin paint may give relief, but watch must be kept for intolerance to this strength of application.

X-ray therapy.—Many of these cases, however, will require some form of irradiation, X-rays being probably the most effective treatment available in a certain proportion of cases, although, in a not inconsiderable percentage of cases, I have not found the relief to be as permanent as some claim it to be, whilst in others there is no response whatsoever. On no account must X-ray therapy be persisted in to a stage where there is any risk of radiodermatitis. Thorium-X has its advocates, but in pruritus ani I have been disappointed with the results.

Tattooing of the area with red sulphide of mercury, and various *minor surgical procedures* have their proponents but I have long ago given up any I ever tried, although I confess I have not tried the tattooing and feel no urge to do so, on æsthetic grounds, if no other.

Opinions differ as to the effects of *dieting*, but many advocate the exclusion of spices, condiments, alcohol, tea, coffee, and Bettley (1949) records some cases in which coffee alone caused pruritus ani. Bettley also reports successes in treatment by a "lactic" regime (a pint of sour milk, two ounces of cream cheese and two teaspoonsful of lactic oats per day).

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TREATMENT OF INCONTINENCE IN THE ELDERLY

INCONTINENCE of urine is one of the great problems among the elderly and chronic sick, occurring in 18.6 per cent. of 701 such patients examined by McEwan and Laverty at Bradford (1949). In some cases, this symptom is preceded by a period during which there is increased frequency or precipitancy of micturition. Its mechanism can best be understood by a study of normal bladder function.

MECHANISM OF MICTURITION

Physiologically, the bladder is a distensible reservoir under the control of the central nervous system. There is a reflex arc in the 2nd, 3rd and 4th sacral segments of the spinal cord, governed by inhibitory impulses from the cerebral cortex. As urine accumulates in the bladder, impulses pass to the spinal "centre", but these are inhibited by the brain, so that the bladder gradually accommodates itself to the volume of fluid. At a certain level (about 300 to 400 ml. of urine), however, the sensation of increased tension reaches consciousness and further inhibition must be performed voluntarily, accompanied by contraction of the perineal muscles. When micturition occurs, the inhibition is removed, efferent impulses pass to the bladder, contract the wall of the organ and relax the sphincters.

The investigations of Wilson (1948) have shown a disturbance of this mechanism in patients with incontinence. Using cystometric methods, he found that old people with increased frequency and precipitancy had an over-irritable reflex arc, combined with diminished bladder sensation for tension. Hence there was a tendency for the organ to contract before there was any conscious desire for micturition. When the escape from cortical control became complete, incontinence occurred. This was, in effect, a return to the infantile state in which a certain amount of urine in the bladder automatically caused reflex contraction and voiding. Any condition which might give rise to increased irritability of the local reflex, or which might sever the link between cerebral cortex and local centre, therefore favoured the onset of incontinence.

Factors increasing reflex irritability of bladder

Infections of the urinary tract
Congestion of the bladder
Presence of residual urine
Senile vaginitis

Factors diminishing cortical control of bladder

Structural lesions of brain or spinal cord (e.g., cerebral thrombosis, disseminated sclerosis)
Psychological states

MANAGEMENT OF INCONTINENT PATIENTS

The first essential is to investigate the various factors mentioned above and to treat them when possible. When there is some urinary infection, sulphonamide drugs will help to eradicate or diminish one of the factors. Stilbœstrol, or other œstrogens, in cases in which the vaginal wall has shown senile vaginitis, seems to

diminish irritability of the bladder reflex to a certain degree. The presence of residual urine associated with an enlarged prostate or cystocele will raise the question of treatment for the primary condition.

The second line of attack is to give the patient a chance to empty the bladder at two- to three-hourly intervals. Wilson has shown that incontinent patients do not empty their bladder completely during micturition, but leave a small amount of residual urine behind. Hence it may be said that the bladder of an incontinent patient is never really full, nor yet really empty. Since the organ contracts and voids itself at the stage when it only contains about 100 ml. of fluid, the need for frequent bedpan or bottle becomes obvious.

If the patient is in hospital, distension of the bladder with fluid can be employed as a form of treatment. The results of this method are variable, however, and are most successful when the patient is intelligent and cooperative. For a description of the technique the reader is referred to Wilson's original article in the *Lancet* (1948). There is a certain class of old person who is incontinent while in bed, but not when up and about. When these folk are taken to the lavatory at regular intervals there is no trouble with them. Another group show incontinence under mental stress or strain. Since the immediate cause of incontinence is often the lack of sense of bladder tension, coupled with uninhibited contractions of the organ, this is understandable.

Most incontinent patients sooner or later develop reddening of the skin over pressure points, which sometimes goes on to actual bedsores. It has been suggested by Cooke that this process is due to the action of *Bacillus ammoniagenes*, and that when this has been inhibited, there is much less chance of excoriation. At the New York Medical College, the drug "diaperene" (a quaternary ammonium compound) has been used for this purpose with promising results (Nagamatsu *et al.*, 1949). Diaperene may be employed as a 1:5000 solution for wet dressings on an infected or ulcerated surface; as a powder to impregnate dry dressings; as an ointment; or it can be made into tablets. In the series mentioned, 23 cases which were either incontinent or else leaking urine from operation wounds or fistulæ, there was improvement in the skin condition in all, some healing completely. This new approach to the problems of the bedsore deserves an extensive trial. "Diaperene" is made by Rohm and Haas of Washington Square, Philadelphia, U.S.A.

Patients suffering from senile dementia or cerebral lesions may become incontinent of fæces. In these cases the basis of treatment should be a simple enema, given twice a week. When there is involuntary action of the bowel between these events, it is sometimes advisable to administer small doses of chalk and opium in order to keep the patients constipated between enemas. If the patient is at home, the problem of soiled linen will otherwise become impossible to solve.

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NOTES AND QUERIES

"Baggy Eyes"

QUERY.—During the last few years I have come across many people with what is commonly known as "baggy eyes". The condition is not particularly confined to middle-aged people, but is seen in those in their early thirties, and of varying occupations, that is, manual as well as mental work, Has worry or overwork anything to do with it? Can the condition be cured or avoided?

REPLY.—The condition referred to is well known, but its causation, and therefore rational treatment is obscure. Major causes, such as nephritis, gross cardiovascular disease and myxœdema are easy to exclude (when thought of). I have more than once been told by oculists of great experience that uncorrected errors of refraction never cause this trouble. Allergy cannot be invoked because the condition is not spasmodic and occasional, but persistent. There is not at present any evidence that it is a sub-deficiency state. I pose the following factors: minor degrees of peripheral venous stasis, fatigue (both physical and mental), lack of fresh air and of sleep, anxiety, and in some cases a physiognominal, and perhaps familial, tendency. If it be advanced that these suggested causative factors are elusive and lack exact definition, it must be remembered that this particular situation probably favours a sub-œdematous change more than any other in the body. So that "baggy eyes" are found, again and again, to be indicative of little more than that the patient is "out of condition". Inquiry as to why, will generally elicit some clue upon which to base treatment.

LORD HORDER, G.C.V.O., M.D., F.R.C.P.

Chronic Alcoholism

QUERY.—I have under my care a female patient aged forty who is a dipsomaniac. She consumes about half a bottle of rum daily, with intermissions of a few days. Her mental condition is deteriorating, although when she is comparatively normal she has a good brain. Could you advise a course of treatment suitable for general practice?

REPLY.—This woman, who daily consumes half a bottle or so of spirits, is a "chronic alcoholist", not a "dipsomaniac", and the prognosis is correspondingly grave. Such a case has passed the stage at which the general practitioner can hope for a happy outcome. Unless restrained in an institution the patient will continue drinking by every crafty device at her disposal, but will deny that she is so doing. The moral and mental deterioration will be progressive and is likely to reach the stage of Korsakow's syndrome. Apart from attention to general hygiene the only known therapy consists in the administration of large doses of vitamin B complex.

A. F. CARVER, M.D., D.P.M.

Atrophy of Breasts Following Lactation

QUERY.—Is it true that lactation causes permanent decrease in the size of a woman's breast, and also loss of "shape"? I have observed this on numerous occasions in slim women after one and two pregnancies. Is there any treatment?

REPLY.—Atrophy of the breasts occurs quite commonly after lactation. The explanation is a matter for speculation. Some authorities have stated that during lactation both ovarian hormones are produced in small amounts and the cessation of lactation therefore leaves the gland in a state of quiescence. The evidence upon which this statement is based is somewhat incomplete, and the explanation does not account for the fact that post-lactational atrophy occurs in a minority of women. Another suggested explanation is that during the phase of activity of the breast there is a crowding-out of the fibrous stroma by the lactating lobules. This simpler explanation appears to be the more likely one.

Loss of shape of the breasts is a different problem. It usually happens as a result of pregnancy, whether or not lactation occurs. Vain women occasionally refuse to suckle their children because they fear a deterioration in the shape of their breasts, and are punished by finding that their breasts become pendulous just the same. Conversely, the few women in my experience whose breasts have retained their shapeliness have all of them suckled their infants for a reasonable period. The loss of shape is due to the stretching of the connective tissue of the breast during the phase of hypertrophy.

The treatment of post-lactational atrophy is unsatisfactory. I have never seen any good come from any form of treatment. If the first explanation given above were correct, the inunction of ointment containing an œstrogen and progesterone should in theory be effective. Apart from plastic surgery there is no treatment for loss of shape.

RAYMOND GREENE, D.M., M.R.C.P.

Treatment of Eunuchoidism

QUERY (from India).—I have a patient, aged thirty-three (a Parsee), with eunuchoidism. He has an unbroken voice and a hairless chin and

has to suffer, as you may well guess, the slings and arrows of thoughtless remarks from all kinds of people. He is an intelligent and plucky fellow, and is worth helping. Will a man of this age benefit from a course of chorionic and/or serum gonadotrophins and testosterone propionate? By benefit I mean, first and foremost, a permanent change in his voice and a reasonably hairy chin; and secondly, although this is not so important to him, is he likely to benefit sufficiently from treatment to be able to marry and have children?

REPLY.—Because of the patient's age the gonadotrophins are unlikely to have any useful effect. Substitution treatment with testosterone is, on the other hand, well worth a trial. It is likely to produce a change in his voice and an increase in facial and body hair, as well as a more positive approach to life in general. It is almost certain that he will be unable to have children, but his penis should increase in size and he will probably experience erections and be able to achieve intercourse. The hormone can be given by mouth as methyl testosterone, in tablets or linguets, 25 mg. three times a day; by intramuscular injection as testosterone propionate, 50 mg. twice a week, or by implanting six 100 mg. tablets subcutaneously. It is suggested that intramuscular injections be tried for two months so that the effect of the treatment can be gauged, and at the end of that time implants may be introduced under the skin one inch below and behind the greater trochanter. They are likely to be effective for some five months and will then have to be replaced by fresh ones.

JOHN S. RICHARDSON, M.V.O., M.D., F.R.C.P.

Congenital Syphilis

QUERY.—I have a healthy female patient, aged twenty-five, who has one healthy child and has just had a miscarriage; her blood and cerebrospinal fluid were tested last month and were quite healthy. In 1938, when she was thirteen, she was investigated for a pain in the right hip and a Wassermann reaction showed slight fixation; a rep. at was positive. A diagnosis of congenital syphilis was made. In May 1939, after NAB 0.15 g. x 8 and bismuth 0.1 g. x 10, W.R. = slight fixation. She was then given NAB 0.15 g. x 4 and bismuth 0.1 g. x 4, and after this she defaulted. This girl is the eldest of six sisters. Her mother denies (to her daughter) that syphilis was ever present. The hospital records (which are incomplete) in 1938 showed that the W.R. of the mother and of the second sister were negative, although for some reason a diagnosis of syphilis was made in the case of the mother. If my patient ever had congenital syphilis, do you consider it possible any of the sisters have it? Outwardly they are all healthy I am told. Is my patient justified in getting blood tests done on her sisters, either unknown to the mother or otherwise? Incidentally, the mother has remarried since the birth of the last child. I do not know the cause of her first husband's death.

REPLY.—This problem seems to be divided into two parts: (1) did the patient really suffer from congenital syphilis? (2) should her sisters have serum tests for syphilis?

(1) The evidence in favour of a diagnosis of congenital syphilis in the patient is very slight; a doubtful followed by a positive W.R. and the (vague) symptom of pain in the hip, of themselves, by no means justify such a diagnosis. Eight injections of NAB 0.15 g. and ten of bismuth 0.1 g. would not be likely to convert a positive W.R. to doubtful; such treatment was very inadequate. The fact that the patient's blood and cerebrospinal fluid are both negative now is also against the diagnosis. Much depends upon where the serum tests were done; if not in an approved laboratory, they are definitely suspect. The facts that the mother denies syphilis (although she must have had syphilis if her daughter had a congenital infection), and that her and her second daughter's serum tests were both negative, are also against the diagnosis. To sum up, one would say that in all probability the patient did *not* have congenital syphilis.

(2) Obviously it would be wise for the sisters to have their bloods tested and a clinical examination as well. Much depends upon their outlook and common sense, but if the patient could call a round table conference of all the sisters and explain the position, she could at least feel she had done her duty and so salve her conscience. Parenthetically it is well known that when a syphilitic woman has a number of pregnancies, successive children are less and less likely to be infected, so that even if the mother did have syphilis some or all of the sisters are likely to have escaped infection. On the other hand, if the patient feels that broaching the subject to her sisters would cause them much pain and nervous shock, little harm is likely to be done by saying nothing. The non-cooperative attitude of the mother would seem in any case to justify the patient in doing what she thinks best for the welfare of her sisters.

T. E. OSMOND, M.B., M.R.C.P.

Vaccinia Following Revaccination

QUERY (from S. India).—About twelve years ago I was, for the first time, revaccinated. Ten days later I developed generalized vaccinia, but there was no reaction whatsoever at the site of

ccination. Later I learnt from my mother that during my primary vaccination also I had had a generalized reaction in addition to a local one. Last month I had an attack of smallpox. The course was mild and scabs were fully formed in just over a week after the appearance of the rash. The majority of lesions, except over the face, head and back, were abortive and formed scabs straight from the papular stage.

Due to the prevalence of smallpox in this place I had my four months' old boy vaccinated (this child was not in my house at the time of my illness). He had a good local reaction but also developed generalized vaccinia. He had been having seborrhœa of the scalp, and the skin over the cheeks was red and itching for a few weeks before vaccination, which would have been postponed but for the prevalence of smallpox in the locality. The grandparents of this child, on the mother's side, are both subject to asthma and eczema, but the mother is quite free. My first child used to have attacks of wheezing during the first year of life but is now free. This child reacted normally to the primary vaccination.

What is the reason for this kind of reaction? Is this tendency inherited? Has the family history of allergy anything to do with it? My own family have been absolutely free from allergy. Am I to be considered to have been hypersusceptible to smallpox? Now that I have had an actual attack could I consider myself immune to smallpox in the future? What course would be advisable regarding revaccination of my child in the future?

REPLY.—When a vaccination "takes", in addition to the local reaction there is always some degree of systemic invasion by the virus, usually too light to give rise to vesiculation of the skin. In rare instances—perhaps about 1 case in 50,000 vaccinations—skin lesions result and may even resemble in distribution and extent those of smallpox. In a lesser degree of infection, vesiculation may be limited to the neighbourhood of the site of vaccination. The explanation appears to be that these persons have an abnormal susceptibility to the virus, which therefore "throws back" to a primitive characteristic normally kept under by the natural resistance of the subject. It seems reasonable to suppose that such persons would also be hypersusceptible to smallpox.

The occurrence of generalized vaccinia in a father and a son is interesting, but in general the excessive susceptibility appears to be an individual and not a familial trait. In a person otherwise of good health, a family tendency to asthma and eczema should not increase the liability to generalized vaccinia.

The highest degree of acquired immunity to smallpox is that provoked by an attack of the disease, but even this is not absolute and depends upon the innate ability of the subject to immunize himself. Undoubted second attacks of smallpox are met with. For example, I saw a most severe case of confluent smallpox in a man who had been a patient in the same smallpox hospital fifteen years before. The patient's statement on admission was confirmed by the hospital records, and, moreover, mixed up with the existing rash, typical scars left by the first rash were clearly visible. The attack ended fatally.

The answer to the query regarding the future revaccination of the child is that this would depend upon local circumstances, bearing in mind that smallpox is an infinitely more dangerous infection than is generalized vaccinia.

SIR WILLIAM MACARTHUR, K.C.B., D.S.O., M.D., F.R.C.P.

Treatment of Psoriasis

QUERY.—May I ask your help in the treatment of a rather intractable, extensive, and long-standing case of psoriasis? A month ago there was a severe exacerbation and the whole body was covered by these patches. Treatment followed was on the lines recommended in "Skin Diseases in General Practice" by Ray Bettley. I am using oil of cade, 20 parts, but have not yet started on chrysarobin. My difficulty is that while the patches in the upper half of the body are clearing, new papules are appearing in the area that had been cleared. In the lower half there are black patches with red edges that show no fading. The skin on the whole is dry and itchy. How can the new papules be prevented from coming out?

REPLY.—Whilst the removal of existing patches of psoriasis can usually be accomplished, it is notoriously difficult to prevent the development of a fresh eruption. The administration of salicylates by the mouth is probably of some value; either sodium salicylate or salicin may be given in full doses. It is advisable to avoid arsenic while active lesions are still appearing. Rest in bed is helpful during this stage. Some form of non-specific protein shock sometimes seems to help the eruptions, and in this case it would be a good plan to give autohæmotherapy for a few weeks. It must be admitted, however, that we know very little about the prevention of fresh patches and in many cases it seems that the phase has to work itself out. During this period, local treatment should be continued, although it is usually advisable to proceed with caution, avoiding the stronger remedies until fresh lesions have ceased to appear.

F. RAY BETTLEY, M.D., F.R.C.P.

PRACTICAL NOTES

Hyaluronidase in Prevention of Heparin Injection Pain

THE pain subsequent to repeated subcutaneous injection of heparin has been successfully circumvented by M. S. Tuchman and S. E. Moolten (*American Journal of the Medical Sciences*, February 1950, **219**, 147) by the infiltration of the injection site with hyaluronidase before administration of the heparin. At the beginning of the trial use of hyaluronidase a freshly prepared solution for each infiltration (1 mg. of hyaluronidase powder to 100 ml. of sterile physiological saline, sterilized by passage through a Seitz filter) was employed, but later a sterile material supplied in ampoules (containing 150 turbidity-reducing units per mg.) was used. A site on the patient's upper arm or thigh was chosen and 5 ml. of hyaluronidase solution (0.5 to 1 unit per ml.) were given before each injection of heparin, a fresh site usually being used for each. The hyaluronidase was given subcutaneously and slowly, a no. 23 or 24 gauge needle being inserted rather deeply and left *in situ*, so that the heparin solution could be delivered through the same needle, about three minutes being taken for its injection. In some instances a site previously utilized was again used for injection of heparin two or three times in succession within a period of twelve hours without infiltrating additional hyaluronidase. There was practically no discomfort to the patient, and little or no pain. The absorption rate and coagulation times were found to be "almost identical with those produced by intermittent intravenous injections of heparin at the same intervals and in similar dosage". In one case treated, the hyaluronidase infiltration proved effective in aiding rapid resorption of a large painful hæmatoma. It is claimed that "the procedure is relatively simple and easily carried out by the nursing staff".

Symphathetic Nerve Block for Herpes Zoster

ACCORDING to L. M. Ferris and G. H. Martin (*Annals of Internal Medicine*, February 1950, **32**, 257), "regional sympathetic nerve block is a simple and safe procedure which can usually be performed in the out-patient clinic. Its use in the treatment of certain painful syndromes is advocated and is the procedure of choice in the treatment of herpes zoster". In the case of herpes zoster about the face and neck, procaine block of the stellate ganglion was carried out, through the anterior approach, using 8 ml. of 1 per cent. procaine hydrochloride. When the thoracic and lumbar segments were involved paravertebral block of the sympathetic ganglia was performed, blocking the involved ganglion and one or two segments above and below that. In lesions of the lower extremities, lumbar ganglia I to IV were injected, using 8 ml. of 1 per cent. procaine hydrochloride at each site. Of 20 patients seen in the early stages of the disease, 15 were "immediately and completely relieved of pain" by one sympathetic block. The remainder required a second block, usually two days after the first one. Of two patients with post-herpetic neuralgia, who were not seen until four weeks after the onset of herpes, one obtained "complete and lasting relief" after two blocks. The other, who had facial herpes, received no relief from two blocks of the stellate ganglion, but subsequently was completely relieved by the intravenous injection of tetraethylammonium bromide.

Conjunctival Ecchymoses in Malaria

IN reporting nine cases of conjunctival ecchymoses in malaria in British subjects in India, D. S. Short (*Journal of Tropical Medicine and Hygiene*, March 1950, **53**, 54) draws attention to the fact that this is apparently the first time this complication has been reported in India. The ecchymoses usually developed between the third and seventh days of the illness and rapidly spread to cover the lower half of the sclera. In four cases both eyes were affected, whilst in three there was bleeding from other sites: epistaxis in one, a purpuric eruption in another, and severe hæmoptysis in the third. In one of the cases a full examination of the blood was made, and bleeding and coagulation times and clot retraction were within normal limits, and platelets were abundant. All responded well to mepacrine. There was no evidence that drugs or concomitant infection played any part in the causation. As vomiting was a marked symptom in all cases, it is considered that this may have precipitated the rupture of a conjunctival blood vessel in some cases, but certainly not in all, as in some the vomiting had abated before the ecchymoses appeared. It is concluded that "the hæmorrhages in these cases were caused by the malarial parasite, which is known to be capable of producing capillary endothelial damage with embolism and rupture of small vessels".

Small Continuous Doses of Dicoumarol

As a result of their experience with 37 patients, L. Epstein and A. Nørholm-Pedersen (*Acta medica scandinavica*, 1950, **136**, 351) claim that

mall repeated doses of dicoumarol provide a ore constant reduction in the prothrombin dex than the large intermittent doses which are ually employed. The prothrombin index was termined by Lehmann's method, and a zone tween 20 and 50 was chosen for the pro-rombin index "as this zone represents a thera-utically effective reduction of the prothrombin ontents and at the same time does not involve e risk of serious hæmorrhage". The best re-lts were obtained with small maintanance oses of 20 mg. of dicoumarol two to four times ily, the precise dosage depending upon the dividual response. It is claimed that with this osage fluctuations in the prothrombin time are mall and easily controlled by slight alterations dosage. When the prothrombin index ap-roaches 20, treatment is stopped for twenty-ur to forty-eight hours, and then renewed ith smaller doses. A further advantage claimed r this method is that daily estimations of the rothrombin index are not necessary once the sired level has been reached.

Estrogen Absorption in Male Chemical Plant Workers

An examination of fifty men working with ixed œstrogens in a large chemical plant in Montreal revealed that 5 of the 50 workers had eveloped toxic symptoms (G. H. Fisk: *Canadian Medical Association Journal*, March 950, **62**, 285). The symptom complained of in ll five cases was gynæcomastia; one or both reasts were enlarged and painful, with a alpable and freely movable nodule, but no dis-harge and no pigmentation. Further inquiry howed that the patients had slight loss of ibido, although there was no instance of true mpotence and no atrophy of the genitalia. eneral physical examination was otherwise egative; there was no loss of weight and no bnormality of the blood counts. Urinary assays or œstrogens, however, were greatly raised: .298 mg. to 0.400 mg. per twenty-four hour ample, i.e. ten times the normal average for ales. In all cases there was return to normal fter ceasing work with œstrogens for one to wo months. No active treatment was given. nquiry revealed that the men affected had eglected the routine precautions and were etting their hands contaminated with the strogen material, and percutaneous absorption nd ingestion of material on the fingers had ccurred. The average length of exposure was bout six months; there was no evidence to ndicate that any particular physical type was ore susceptible than another, both masculine nd feminine types of build being among those ffected. It is stated that "Carelessness is the one common factor in these cases and far more important than sensitivity". Routine preventive measures in force at the factory in question included: careful instruction of employees handling the œstrogen material; showers, gloves, masks, overalls, exhaust fans, and air-conditioning. Despite this, carelessness among workers may lead to toxic symptoms, as shown in the quoted report.

Treatment of Ulcerative Stomatitis

That the remarkable effects of the antibiotics should not lead to the neglect of certain classical methods of proved efficacity is pointed out by L. Rouques (*Presse Médicale*, February 25, 1950, **58**, 207) in recording the excellent results obtained by Tassovatz (*Archives français de Pédiatrie*, 1949, **6**, 604) in the treatment of a number of child refugees with ulcerative stomatitis during an epidemic in Yugoslavia in 1942. The method employed was freezing the gums with an ethyl chloride spray for a few seconds once daily, for several consecutive days. Most of the children were treated in the chronic stage, after isolation and lavage of the mouth with disinfectants had failed to clear the condition. Some of the cases, however, were acute. Thirty children so treated were cured within six to eight days. Another method employed was lavage of the mouth with 1 per cent. oxygenated water for ten minutes, every two hours day and night. Forty children so treated were cured in eight to ten days. Using one or other of the methods, Tassovatz obtained amelioration of the condition in three days and complete cicatrization of the ulcerations within eight to ten days. All the cases treated were severe and resistant.

Provocative Diet in Diagnosis of Food Allergy

"The provocative diet is a positive aid in the identification of specific food allergens and in the intelligent management of patients with real food intolerance", write H. L. Lee and T. L. Squier (*Journal of the American Medical Association*, February 4, 1950, **142**, 318). Unless the patient's history, or observation of the individual case, contraindicates its use, the following diet is employed:—

> Wheat, milk, egg, beef, orange and potato are eaten exclusively for a trial period of approximately one week. In addition to being the major constituents of a normal diet, these foods are those most often responsible for food allergy. When any sensitivity exists to any of these major foods, symptoms are usually evident before the end of the trial period and may increase in severity. When, however, the diet can be taken without any evidence of increased symptoms it may be assumed that the foods in question have no importance in the causation of the symptoms.

Not only may ingested foods cause allergic symptoms, but they may also aggravate those

caused by inhaled antigens. Both foods and inhalants can cause rhinitis, asthma, urticaria, malaise, lassitude or headache. It is emphasized that when exacerbation of symptoms occurs with the provocative diet, further observation and trial are necessary before finally incriminating a food factor, particularly when exposure to pollens or inhalants has occurred at the same time. The diet "provides a satisfactory method for obtaining positive evidence of tolerance for basic foods. The extreme depletion which all too often results from ill-advised and long-continued elimination diets will never occur if provocative diets are used".

Treatment of Trichomonas Vaginalis Vaginitis

WHEREAS the pH of the normal vaginal secretions is 4.0 to 4.5, with lactobacilli present and muco-epithelial discharge, in the vagina infected by *Trichomonas vaginalis* the pH of the secretions is above 5.0 (usually 5.5 to 6.5), lactobacilli are absent, and various other abnormal floræ are present, including leucocytes. On the basis of these findings, and of the fact that the trichomonad does not thrive in the pH of normal vaginal secretions, J. F. Fiorino, L. Arrigoni, and G. A. Tozer (*American Journal of Obstetrics and Gynecology*, February 1950, **59**, 432) have treated a large series of cases by changing the reactions of the vaginal fluid to within normal range. The following acid douche was first employed.

Glycerin	4 ounces (114 ml.)
Lactic acid	½ ounce (14.2 ml.)
Phosphoric acid	½ ounce (14.2 ml.)
Solution phenylmercuric nitrate 1:1000 q.s.	1 pint (570 ml.)

One tablespoonful of this solution is added to 1 quart (1 litre) of warm water and used as a douche morning and evening. The pH of the solution is 3.6

The use of the douche was followed by insertion, deeply into the vagina, every six hours and two at night, of a 2.75 g. tablet made from the following formula:—

Potassium phosphate monobasic	200 ml.
Phosphoric acid 85 per cent.	15 ml. (or q.s. to pH 3.6)
Carbamide hydrochloride	0.04 ml.
Beta lactose	200 ml.

The treatment has been used in 300 cases of *Trichomonas vaginalis* with vaginal reactions, before treatment, of 5.2 to 6.6 (average 6), which in most instances dropped in less than one week to 4.2, with disappearance of trichomonads, reappearance of lactobacilli and epithelial cells, and showing only scattered leucocytes and abnormal bacteria in the vaginal secretion. The purulent discharge, inflammation, and pruritus "disappeared concomitantly with the re-establishment of normal vaginal conditions". It is stated further that "of the 279 of the original 300 patients who returned for re-examinatio 268 were cured without recurrence, and th remaining eleven were cured after an additiona period of treatment following recurrence".

The "Ether Sign" For Determination of Death

AT the National Academy of Medicine, Par recently, Professor Balthazard described th "ether sign" for the determination of dea (*Médecine et Hygiène*, February 1, 1950, 35). In cases of doubt, 1 to 2 ml. of ether a injected into the skin: if the ether diffuses i the tissues, death is only apparent, and activ measures for reanimation should be institute immediately; if, however, the ether spurts ou when the needle is withdrawn, then death ha taken place and autopsy, if required, can be pro ceeded with. It is stated that the test entails n danger to the subject; in fact, it constitutes th first means for setting about the attempt t bring him to life. The response to the test i immediate, and it is claimed that during period of twenty-five years in all cases in whic the ether sign has been positive it has been im possible to reanimate the subject.

Hyperhidrosis of the Feet

SOME useful formulæ for use in the treatment o hyperhidrosis of the feet are given by K. H Campbell Jones ("The Practice of Chiropody" Angus and Robertson, 1950.):—

Solution of coal tar or coal tar detergent	1 ounce (28.4 ml.)
Salicylic acid	60 grains (4 g.)
Rectified spirit or methylated spirit	to 4 ounces (114 ml.

Swab over feet and between toes twice daily.

After application of the above lotion, the fe should be dusted with the following powder—

Boric acid	240 grains (16 g.)
Salicylic acid	60 grains (4 g.)
Tannic acid	60 grains (4 g.)
Starch	1 ounce (31 g.)
French chalk	to 4 ounces (124 g.)

Dust over feet, between toes, and in socks and sho daily.

Another cooling lotion, for use when the con dition has improved, is:—

Cologne spirit	3 ounces (85 ml.
Methyl salicylate	120 minims (7 ml.
Menthol	25 grains (1.5 g.)
Tragacanth mucilage	sufficient to thicke
Distilled water	to 8 ounces (227 ml.

Rub in, then powder, twice daily.

The following may also be employed: 1 to per cent. solution of sodium hexametaphosphate twice daily; salicylic acid, 2 to 3 per cent. i eau de Cologne; 10 per cent. formaldehyd solution, but this must be used with care. Othe therapeutic measures recommended includ antiseptic foot baths; contrast baths; infra-re rays.

REVIEWS OF BOOKS

e Biology of Mental Defect. By LIONEL S. PENROSE, M.D. With a Preface by PROF. J. B. S. HALDANE, F.R.S. London: Sidgwick and Jackson, Ltd., 1949. Pp. xiv and 285. Illustrated. Price 21*s.*

this notable book Professor Penrose deals h the etiology of the different types of mental fect and discusses the social significance of se of low intelligence. It contains a historical oduction and many diagrams and figures, as ll as photographic illustrations and a full bliography. Recent advances in knowledge are scribed fully, particularly what is known re-rding the hereditary transmission of different rms of defect. Of theoretical interest also is fact that noxæ, such as that of scarlatina or protozoon known as toxoplasma, can affect fœtus *in utero*. The author also deals with remarkable form of mental defect called enylketonuria, which is transmitted by a re-ssive gene and results from the faulty meta-lism of certain breakdown products of a pro-n. With regard to the social problems in-lved, he discusses fully whether a real decline intelligence is taking place in the population d records a verdict of not proven. One also rns that a high proportion of juvenile de-quents are mentally defective and that it is ice as costly for them to be treated in prison in a mental defective institution. The future ssibilities of prevention are also dealt with, d there is a summary of treatment. He em-asizes that the mental defective will always be th us and that the level of cultural develop-ent of a particular community may be gauged the manner in which it deals with its back-rd members. This book is no less essential r the practitioner and social worker than for e specialist.

ychology and Mental Health. By J. A. HADFIELD, M.A., M.B., CH.B. London: George Allen and Unwin, Ltd., 1950. Pp. 444. Price 18*s.*

AINST a background of the familiar theme of ychogenesis in the neuroses and kindred per-nality disorders, the author expounds his own cial viewpoint and psychotherapeutic tech-que; and he compares his principles with those older schools of psychopathology and psycho-rapy. There is little reference to recent fresh proaches to the neuroses, especially the tistical analysis of constitutional traits and jective studies of attributes of the personality modern test procedures. Possibly this ission is intentional; one gets the impression t Dr. Hadfield, in response to requests from those who have enjoyed his lectures, aims to formulate his own point of view, founded on his lengthy experience, rather than to compile a concise or compendious introduction to the subject. There is a tendency to repetition and diffuseness; but those who seek a leisurely and reflective exposition of some psychological aspects of the neuroses will find the book enjoyable and easy to read. It is not intended exclusively for medical readers.

Diseases of the Heart. By CHARLES K. FRIEDBERG, M.D. Philadelphia and London: W. B. Saunders Company, 1949. Pp. xxxii and 1081. Figures 79. Price 57*s.* 6*d.*

THIS textbook is particularly sound in the more practical aspects of cardiology and emphasizes the functional aspects of heart disease as opposed to the structural. Every care has been taken to ensure that the work is up to date: aureomycin and the use of ACTH and compound E in acute rheumatism receive due attention. An excellent example of the balanced approach to a problem, characteristic of the book, is the section on subacute bacterial endocarditis, where considerable space is given to the discussion of the bacteriology of the disease in relationship to penicillin therapy. This is a full, yet discriminating, study of cardiology and one which will prove of value to practitioners as well as to undergraduates and postgraduates.

Diagnostic Radiology. By G. CLAESSEN, M.D. Copenhagen: Einar Munksgaard; London: William Heinemann (Medical Books), Ltd., 1949. Pp. 411. Figures 396. Price 60*s.*

As indicated in the foreword by J. W. McLaren this book is intended primarily for medical students and practitioners, for which purpose it was designed by the well-known Icelandic radiologist the late Dr. Claessen. It is, however, rather long to be regarded as such, and there is a slight lack of balance whereby certain conditions in the alimentary tract could have been more adequately illustrated. These include cardiospasm, œsophageal ulcer, hiatus hernia, and diverticulitis, whereas cerebral tumours receive a rather lengthy description, and rare conditions such as osteopoikilosis are included. These, however, are minor criticisms of a book which is admirably translated and contains remarkably few of the defects which are usual in a first edition and a translation. The illustrations are well selected and the text concise and readable. Those to whom an introduction to radiology is necessary

will find this a most useful volume. The arrangement is to be commended and the Danish publishers can be well satisfied with the quality of this production.

The Clinical Management of Varicose Veins. By DAVID WOOLFOLK BARROW, M.D. London: Cassell and Company Ltd., 1949. Pp. xii and 155. Figures 58. Price 25*s*.

THIS is an admirable book and should be in the hands of all those undertaking the treatment of varicose veins and their complications. This is a condition which is liable to be left to junior members of a hospital staff, whereas it is a subject of such importance and is so common, that it well repays time and energy. In this book attention is drawn to the physiology of the veins of the lower limb, and there is a clear review of the pathology. The treatment described is full and detailed. If the indications for the various types of operation are followed through, a great deal will be achieved in reducing the disability of this condition. It is a book to be strongly recommended to surgeons as well as to general practitioners.

A Histology of the Body Tissues: With a Consideration of their Functions. By MARGARET GILLISON. Edinburgh: E. & S. Livingstone Ltd., 1950. Pp. xiv and 220. Figures 103. Price 15*s*.

THE author and publishers are to be congratulated on the production of this excellent primer. The unique way in which the book bridges the microscopical anatomy of the tissues of the body and their physiological functions will earn the commendation of most teachers and the thanks of any beginner in the study of animal biology. A concise, unambiguous text is splendidly illustrated with 103 monochrome reproductions of "ideal" sections and drawings which cannot fail to whet the interest of the reader. Form and function are ideally integrated. One can only hope that the book's success will be immediate; it cannot reasonably be otherwise.

NEW EDITIONS

Combined Textbook of Obstetrics and Gynæcology, edited by Dugald Baird, M.D., D.P.H., F.R.C.O.G., in its fifth edition (E. & S. Livingstone Ltd., 70*s*.) contains new chapters dealing with stillbirth, infant mortality, and the psychological factors in obstetrics and gynæcology. The importance of physiological reproduction is stressed in the Editor's preface, and he states that "many fœtal deaths are associated with forms of 'physiological failure' rather than with definite pathological processes." The new edition is beautifully produced and illustrated, and should prove a welcome addition to the practitioner's library.

A NEW chapter on the endocrinological and biochemical aspects of rheumatic disease has been added to *The Rheumatic Diseases*, by G. I. Kersley, M.D., F.R.C.P., T.D., in its third edition (William Heinemann (Medical Books) Ltd., 15*s*.). In this chapter are sections on the adrenocortical hormones, cortisone, ACTH, and the polysaccharides and hyaluronidases, and their uses in the different forms of rheumatic disease. Selye's adaptation syndrome, and its rôle in raising resistance, are discussed in the chapter on special treatments.

Mitchell-Nelson Textbook of Pediatrics, edited by Waldo E. Nelson, M.D., in its fifth edition (W. B. Saunders Company, 63*s*.) contains among its contributors many eminent in the pædiatric world. The whole work has been revised and much new material added: in the section on the cardiovascular system there is a useful subsection on congenital heart disease and modern methods of treatment; there is a section on parenteral fluid therapy; a number of new drugs have been included, with their dosage and methods of administration. The new edition is generously illustrated, containing in all 426 figures.

Stern's Applied Dietetics, revised by Helen Rosenthal, B.S., Pearl C. Baker, B.S., and Wilma A. McVey, M.D., in its third edition (Baltimore: Williams and Wilkins Company; London: Baillière, Tindall & Cox, 38*s*.) gives much useful information, first on normal diet for the maintenance of health, and then on specific therapeutic diets. There are also tables giving the food values of different foodstuffs and beverages. As the work was compiled in the United States many of the items included in the diet sheets are unobtainable in Great Britain to-day, but the general dietary outlines should prove helpful despite this restriction.

The Diabetic Life, by R. D. Lawrence, M.D., F.R.C.P., in its fourteenth edition (J. & A. Churchill Ltd., 10*s*. 6*d*.) has been revised to include advances since the appearance of the previous edition in 1944. In his preface the author mentions the availability of insulin and other diabetic necessities under the Health Service, and expresses the hope that the establishment of regional clinics where diabetics can obtain expert supervision may be included in its scope. A section in the Appendix deals with post-war food changes and difficulties.

The contents of the June issue, which will contain a symposium on "Peripheral Vascular Disease", will be found on page lxx.

Notes and Preparations, see page lvii.
Fifty Years Ago, see page lxiii.